Access DB# 65124

# SEARCH REQUEST FORM

**Scientific and Technical Inf rmation Center**

Requester's Full Name: S. Kumar Examiner #: 69594 Date: 11/28/02
Art Unit: 1621 Phone Number 30 8459 Serial Number: 09/776,936
Mail Box and Bldg/Room Location: CM1 7A07 7E12 Results Format Preferred (circle): PAPER DISK E-MAIL

**If more than one search is submitted, please prioritize searches in order of need.**

**********

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

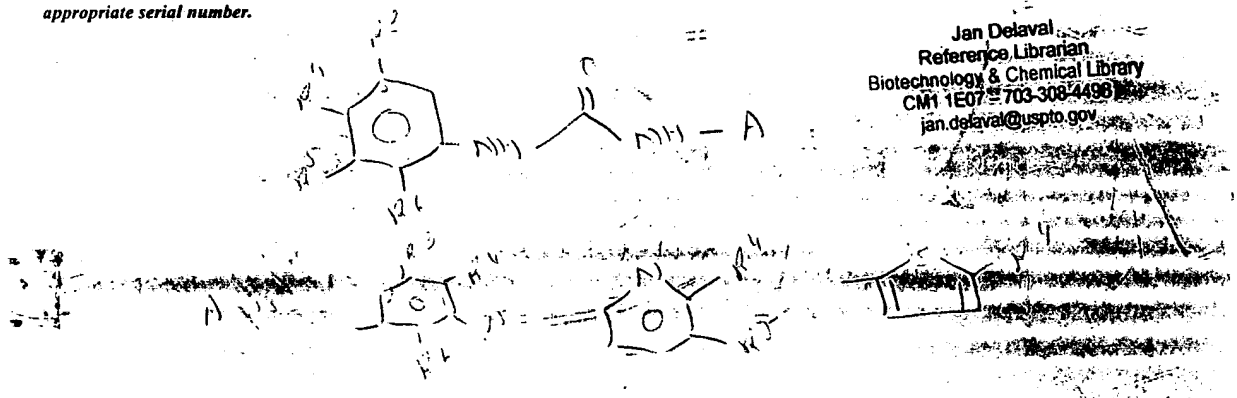
Title of Invention: Inhibitors of [illegible]

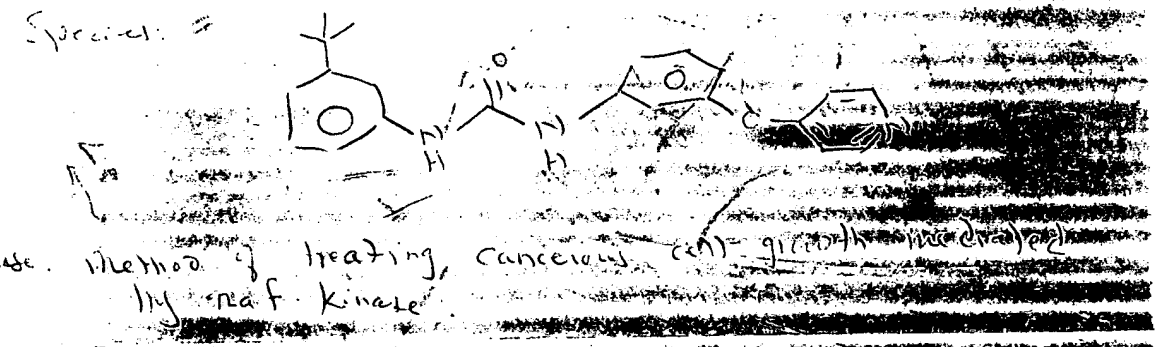
Inventors (please provide full names): Scott Miller et al

Earliest Priority Filing Date: 12/12/1997

***For Sequence Searches Only*** *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4496
jan.delaval@uspto.gov





Use: Method of treating cancer(s) mediated by [illegible] kinase

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Date Searcher Picked Up: 5/2/01
Date Completed: 5/2/01
Searcher Prep & Review Time: _____
Clerical Prep Time: 20
Online Time: + 80

**Type of Search**

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) ✓
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

**Vendors and cost where applicable**

STN ✓
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Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

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=> d his

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L3             2 S L2 AND DIMETHYLETHYL PHENYL
                 SEL RN
L4             0 S E1-E2/CRN

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L5             0 S L3

     FILE 'HCAPLUS' ENTERED AT 09:26:32 ON 02 MAY 2002
L6             1 S L3

     FILE 'USPATFULL, USPAT2' ENTERED AT 09:26:36 ON 02 MAY 2002
L7             0 S L3

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DICTIONARY FILE UPDATES:  30 APR 2002  HIGHEST RN 409303-45-3

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Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d l3 ide can tot

L3   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2002 ACS
RN   228399-53-9  REGISTRY
CN   Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[3-(4-pyridinyloxy)phenyl]-
     (9CI)  (CA INDEX NAME)
FS   3D CONCORD
MF   C22 H23 N3 O2
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER
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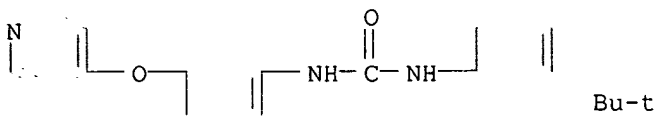


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
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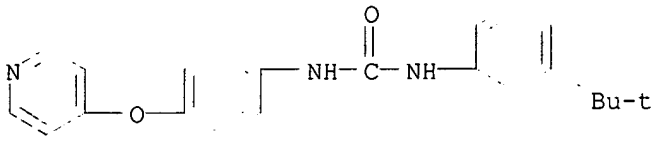
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:58658

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 228399-50-6 REGISTRY
CN **Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]-(9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF **C22 H23 N3 O2**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:58658

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FILE COVERS 1907 - 2 May 2002 VOL 136 ISS 18
FILE LAST UPDATED: 30 Apr 2002 (20020430/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

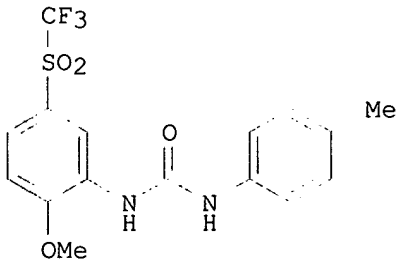
=> d all 16

L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:421642 HCAPLUS
DN 131:58658
TI Inhibition of raf kinase using symmetrical and unsymmetrical substituted diphenyl ureas
IN Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Rodriguez, Mareli; Wang, Ming
PA Bayer Corporation, USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C275-24
ICS C07D213-02; C07D333-02; A61K031-17; A61K031-38; A61K031-44
CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 7
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9932436 | A1 | 19990701 | WO 1998-US26081 | 19981222 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2315646 | AA | 19990701 | CA 1998-2315646 | 19981222 |
| | AU 9919054 | A1 | 19990712 | AU 1999-19054 | 19981222 |
| | EP 1049664 | A1 | 20001108 | EP 1998-963809 | 19981222 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | JP 2001526258 | T2 | 20011218 | JP 2000-525373 | 19981222 |
| | NO 2000003230 | A | 20000821 | NO 2000-3230 | 20000621 |
| PRAI | US 1997-996344 | A | 19971222 | | |
| | WO 1998-US26081 | W | 19981222 | | |

OS MARPAT 131:58658
GI




II

AB The invention relates to the use of a group of aryl ureas ANHCONHB [I; A = certain (un)substituted Ph, pyridinyl, or thien-2-yl groups; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] in treating raf-mediated diseases, and pharmaceutical compns. for use in such therapy. A subset of I are novel and are claimed per se. Approx. 160 invention compds. and numerous intermediates were prepd. For instance, reaction of tolyl isocyanate with 2-methoxy-5-(trifluoromethanesulfonyl)aniline in EtOAc gave title compd. II. In an in vitro raf kinase assay, all compds.

displayed IC50 values between 1 nM and 10 .mu.M.

ST diphenyl urea prepn raf kinase inhibitor; aryl urea prepn antitumor agent

IT Antitumor agents
(Inhibition of raf kinase using sym. and unsym. substituted di-Ph ureas)

IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(gene c-raf; Inhibition of raf kinase using sym. and unsym. substituted di-Ph ureas)

IT 726-17-0P 780-90-5P 843-06-1P 883-62-5P 885-87-0P 5651-77-4P
6337-24-2P 13041-60-6P 13472-85-0P 16588-75-3P 18994-90-6P
27692-74-6P 28232-52-2P 31465-36-8P 32361-76-5P 36089-89-1P
40299-87-4P 51834-97-0P 61500-87-6P 62248-47-9P 62248-51-5P
64064-63-7P 67291-63-8P 70991-08-1P 92575-23-0P 116289-71-5P
135680-03-4P 142596-52-9P 165256-89-3P 178809-75-1P 220000-87-3P
228401-08-9P 228401-09-0P 228401-10-3P 228401-11-4P 228401-14-7P
228401-15-8P 228401-16-9P 228401-17-0P 228401-18-1P 228401-19-2P
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228401-43-2P 228401-44-3P 228401-45-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)

IT 370-50-3P 228399-32-4P 228399-33-5P 228399-34-6P 228399-35-7P
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228399-52-8P **228399-53-9P** 228399-54-0P 228399-56-2P
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228401-07-8P 228401-49-8P 228401-50-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
IT 144378-33-6, Raf Kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
IT 86-84-0, 1-Naphthyl isocyanate 100-11-8, 4-Nitrobenzyl bromide 100-15-2, N-Methyl-4-nitroaniline 100-51-6, Benzyl alcohol, reactions 101-77-9 106-44-5, reactions 106-49-0, p-Toluidine, reactions 108-30-5, reactions 109-00-2, 3-Hydroxypyridine 110-91-8, Morpholine, reactions 123-30-8, 4-Aminophenol 150-76-5, 4-Methoxyphenol 288-32-4, Imidazole, reactions 320-94-5, 2-Nitro-4-(trifluoromethyl)benzoic acid 327-78-6, 4-Chloro-3-(trifluoromethyl)phenyl isocyanate 349-65-5, 2-Methoxy-5-(trifluoromethyl)aniline 350-46-9, 1-Fluoro-4-nitrobenzene 358-23-6, Trifluoromethanesulfonic anhydride 371-40-4, 4-Fluoroaniline 400-74-8, 2-Fluoro-5-nitrobenzotrifluoride 452-80-2, 2-Fluoro-4-methylaniline 453-20-3, 3-Hydroxytetrahydrofuran 498-74-8, 4-Methoxymetanilyl fluoride 551-06-4 585-34-2 585-79-5, 1-Bromo-3-nitrobenzene 620-95-1, 3-Benzylpyridine 622-58-2, p-Tolyl isocyanate 624-28-2, 2,5-Dibromopyridine 626-61-9, 4-Chloropyridine 768-35-4 872-31-1, 3-Bromothiophene 883-99-8 1083-48-3, 4-(4-Nitrobenzyl)pyridine 1121-78-4, 5-Hydroxy-2-methylpyridine 1849-36-1 2033-89-8, 3,4-Dimethoxyphenol 2103-88-0, 2-Mercapto-4-phenylthiazole 3279-07-0, 4-tert-Butyl-2-nitrophenol 3535-88-4, 5-tert-Butyl-2-methoxyaniline 3678-63-5 4548-45-2, 2-Chloro-5-nitropyridine 4556-23-4, 4-Mercaptopyridine 4595-59-9, 5-Bromopyrimidine 6310-19-6, 4-tert-Butyl-2-nitroaniline 6358-07-2 7379-35-3, 4-Chloropyridine hydrochloride 21101-60-0, 4-(4-Nitrophenylthio)phenol 22948-02-3, 3-Aminothiophenol 24424-99-5, Di-tert-butyl dicarbonate 25267-27-0, Iodobutane 29264-35-5 36265-31-3 73322-01-7, 4-(2-Pyridinylthio)-1-nitrobenzene 198077-72-4, 2-Methoxy-5-(difluoromethanesulfonyl)aniline 228401-47-6, 2,4-Dimethoxy-5-(trifluoromethyl)aniline 228401-48-7, 2-Hydroxy-5-(trifluoromethylthio)aniline
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Dixon; US 5470882 A 1995 HCAPLUS
(2) Seto; US 5429918 A 1995 HCAPLUS
(3) Smithkline Beecham Corporation; WO 96/25157 A1 1996 HCAPLUS

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Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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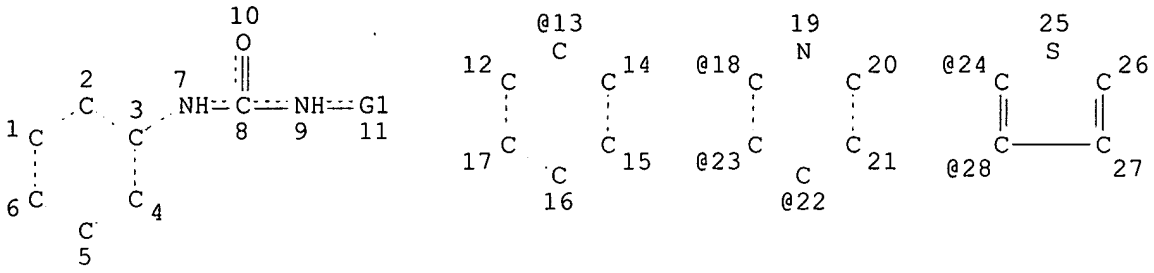
L1 STR

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 75223 ITERATIONS 23426 ANSWERS
SEARCH TIME: 00.00.06

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L2 23426 SEA FILE=REGISTRY SSS FUL L1
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L3 2 S L2 AND C22H23N3O2/MF
L4 23424 S L2 NOT L3

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L5 8315 S L4

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L6 1 S 144378-33-6

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L9 17 S KINASE PHOSPHORYLATING GENE C RAF PROTEIN
L10 574 S L7-L9
L11 7 S L5 AND L10

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L18          197 S E3,E4 AND L5
                 E MILLER S/AU
L19          930 S E3-E36
                 E  MILLER SCOTT/AU
L20          222 S E3-E26
                 E OSTERHOUT M/AU
L21           34 S E3-E5,E7-E9
                 E DUMAS J/AU
L22          458 S E3-E16
                 E KHIRE U/AU
L23           24 S E4-E6
                 E LOWINGER T/AU
L24           23 S E4-E6
                 E RIEDL B/AU
L25           84 S E3,E7
                 E SCOTT W/AU
L26          155 S E3,E22-E27
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L27          153 S E3,E34-E39
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L28          992 S E3-E15
                 E SMITH ROGER/AU
L29          219 S E3-E7
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L30          178 S E3,E16-E20
                 E WOOD JILL/AU
L31           14 S E3-E5
                 E GUNN D/AU
L32           33 S E3,E6,E15,E16
                 E RODRIGUEZ M/AU
L33          942 S E3-E70,E242-E251
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L34         1245 S E3-E34
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                 E TURNER T/AU
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                 E BRENNAN C/AU
L38           74 S E3-E13,E21-E25
L39           18 S L5 AND L19-L38
L40           10 S L16 AND L39
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L41           10 S E3
L42            3 S L41 AND L5
L43            2 S RODRIGUEZ M?/AU AND L5
L44            7 S L39,L42,L43,L18 AND L15
L45            5 S L16 AND L44
L46            2 S L44 NOT L45

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 11:15:08 ON 02 MAY 2002
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FILE COVERS 1907 - 2 May 2002 VOL 136 ISS 18
FILE LAST UPDATED: 30 Apr 2002 (20020430/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

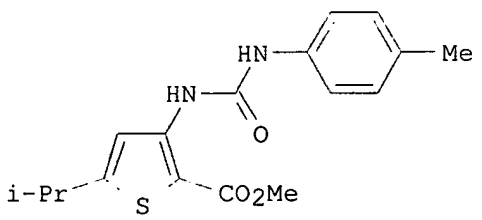
CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d l45 bib abs hitrn tot

L45 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:111513 HCAPLUS
DN 134:163040
TI Preparation of heteroaryl aryl ureas as **raf kinase** inhibitors
IN **Wood, Jill E.**; Wild, Hanno; Rogers, Daniel H.; Lyons, John; Katz, Michael; Caringal, Yolanda; Dally, Robert; Lee, Wendy; **Smith, Roger A.**; Blum, Cheri
PA Onyx Pharmaceuticals, USA; **Bayer** Corporation
SO U.S., 30 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|---|
| PI | US 6187799 | B1 | 20010213 | | US 1998-83399 | 19980522 | <-- |
| | US 2001006975 | A1 | 20010705 | | US 2001-755060 | 20010108 | |
| PRAI | US 1997-126420P | P | 19970523 | <-- | | | |
| | US 1998-83399 | A3 | 19980522 | | | | |

GI




I

AB The title heteroaryl aryl ureas, useful in treating tumors mediated by

**raf kinase** (no data), were prepd. E.g., a multi-step synthesis of the urea I was given. The title compds. such as I are effective at 0.01-200 mg/kg/day.

IT **216573-01-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of heteroaryl aryl ureas as **raf kinase** inhibitors)

IT **216573-03-4P 216573-34-1P 216574-09-3P**
**216574-10-6P 216574-11-7P 216589-05-8P**
**216589-46-7P 216852-73-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heteroaryl aryl ureas as **raf kinase** inhibitors)

IT **144378-33-6, RAF kinase**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of heteroaryl aryl ureas as **raf kinase** inhibitors)

IT **216591-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heteroaryl aryl ureas as **raf kinase** inhibitors)

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

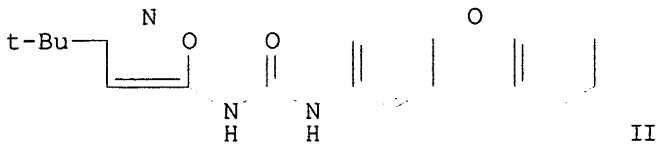
L45 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:425740 HCAPLUS
DN 131:73648
TI Inhibition of **raf kinase** using substituted heterocyclic ureas
IN **Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno**; Paulsen, Holger; **Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.**; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PA **Bayer** Corporation, USA
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9932106 | A1 | 19990701 | WO 1998-US26078 | 19981222 <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2315717 | AA | 19990701 | CA 1998-2315717 | 19981222 <-- |
| | AU 9921989 | A1 | 19990712 | AU 1999-21989 | 19981222 <-- |
| | EP 1047418 | A1 | 20001102 | EP 1998-965981 | 19981222 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | JP 2001526220 | T2 | 20011218 | JP 2000-525097 | 19981222 <-- |

| | | | | | |
|---|---|---|---|---|---|
| | NO 2000003232 | A | 20000821 | NO 2000-3232 | 20000621 <-- |
| PRAI | US 1997-996343 | A | 19971222 <-- | | |
| | WO 1998-US26078 | W | 19981222 | | |

OS MARPAT 131:73648

GI



II

AB A method for treatment of cancerous cell growth mediated by **raf kinase** comprises administration of urea derivs. ANHCONHB [I; A = substituted isoxazolyl, thienyl, thiadiazolyl, furyl, pyrazolyl, etc.; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. .gtoreq.1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-phenyloxyphenyl isocyanate with 5-amino-3-tert-butylisoxazole in methylene chloride and heating at reflux temp. for 2 days gave title compd. II. In an in vitro **raf kinase** assay, I displayed IC50 values of 1-10 .mu.M.

IT **229003-12-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

IT **229002-65-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

IT **227623-30-5P 229002-62-4P 229002-63-5P 229002-66-8P 229002-67-9P 229002-70-4P 229002-72-6P 229002-74-8P 229002-75-9P 229002-76-0P 229002-93-1P 229002-95-3P 229002-96-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

IT **144378-33-6, Raf kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

IT **229003-21-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:421660 HCAPLUS
DN 131:44811
TI Preparation of aryl- and heteroaryl-substituted heterocyclic ureas as **raf kinase** inhibitors
IN **Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno;** Paulsen, Holger; **Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.;** Hatoum-Mokdad, Holia; Johnson, Jeffrey; Redman, Aniko; Sibley, Robert
PA **Bayer** Corporation, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | WO 9932455 | A1 | 19990701 | WO 1998-US26082 | 19981222 | <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| | CA 2315713 | AA | 19990701 | CA 1998-2315713 | 19981222 | <-- |
| | AU 9919055 | A1 | 19990712 | AU 1999-19055 | 19981222 | <-- |
| | EP 1056725 | A1 | 20001206 | EP 1998-963810 | 19981222 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| | BR 9814361 | A | 20011127 | BR 1998-14361 | 19981222 | <-- |
| | JP 2001526269 | T2 | 20011218 | JP 2000-525392 | 19981222 | <-- |
| | NO 2000003231 | A | 20000822 | NO 2000-3231 | 20000621 | <-- |
| PRAI | US 1997-996181 | A | 19971222 | <-- | | |
| | WO 1998-US26082 | W | 19981222 | | | |

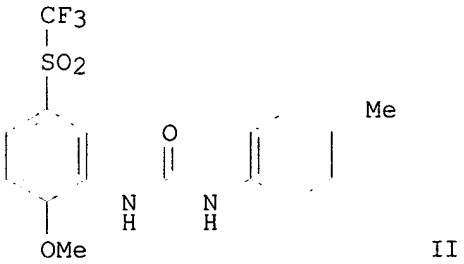
OS MARPAT 131:44811
AB The title compds. ANHCONHB (A = heteroaryl; B = aryl, heteroaryl), **raf kinase** inhibitors, were prepd. E.g., N-(1-phenyl-3-tert-butyl-5-pyrazolyl)-N'-(4-(4-pyridinylmethyl)phenyl)urea was prepd.
IT **227623-25-8P 227623-30-5P 227623-31-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl- and heteroaryl-substituted heterocyclic ureas as **raf kinase** inhibitors)
IT **144378-33-6, Raf kinase**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of aryl- and heteroaryl-substituted heterocyclic ureas as **raf kinase** inhibitors)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:421642 HCAPLUS
DN 131:58658
TI Inhibition of **raf kinase** using symmetrical and unsymmetrical substituted diphenyl ureas
IN **Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Rodriguez,**

**Mareli; Wang, Ming**
PA **Bayer** Corporation, USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9932436 | A1 | 19990701 | WO 1998-US26081 | 19981222 <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2315646 | AA | 19990701 | CA 1998-2315646 | 19981222 <-- |
| | AU 9919054 | A1 | 19990712 | AU 1999-19054 | 19981222 <-- |
| | EP 1049664 | A1 | 20001108 | EP 1998-963809 | 19981222 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | JP 2001526258 | T2 | 20011218 | JP 2000-525373 | 19981222 <-- |
| | NO 2000003230 | A | 20000821 | NO 2000-3230 | 20000621 <-- |
| PRAI | US 1997-996344 | A | 19971222 <-- | | |
| | WO 1998-US26081 | W | 19981222 | | |

OS MARPAT 131:58658
GI




II

AB The invention relates to the use of a group of aryl ureas ANHCONHB [I; A = certain (un)substituted Ph, pyridinyl, or thien-2-yl groups; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] in treating raf-mediated diseases, and pharmaceutical compns. for use in such therapy. A subset of I are novel and are claimed per se. Approx. 160 invention compds. and numerous intermediates were prepd. For instance, reaction of tolyl isocyanate with 2-methoxy-5-(trifluoromethanesulfonyl)aniline in EtOAc gave title compd. II. In an in vitro **raf kinase** assay, all compds. displayed IC50 values between 1 nM and 10 .mu.M.

IT **370-50-3P 228399-32-4P 228399-33-5P**
**228399-34-6P 228399-35-7P 228399-36-8P**
**228399-38-0P 228399-39-1P 228399-40-4P**
**228399-41-5P 228399-42-6P 228399-43-7P**
**228399-44-8P 228399-45-9P 228399-47-1P**
**228399-48-2P 228399-49-3P 228399-51-7P**
**228399-52-8P 228399-54-0P 228399-56-2P**
**228399-57-3P 228399-58-4P 228399-59-5P**
**228399-60-8P 228399-61-9P 228399-62-0P**
**228399-63-1P 228399-65-3P 228399-66-4P**
**228399-67-5P 228399-68-6P 228399-69-7P**

228399-70-0P 228399-71-1P 228399-72-2P
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228399-80-2P 228399-82-4P 228399-83-5P
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228399-87-9P 228399-88-0P 228399-89-1P
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228399-97-1P 228399-98-2P 228399-99-3P
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228400-04-2P 228400-05-3P 228400-06-4P
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228400-43-9P 228400-44-0P 228400-45-1P
228400-46-2P 228400-47-3P 228400-48-4P
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228400-96-2P 228400-97-3P 228400-99-5P
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228401-03-4P 228401-04-5P 228401-07-8P
228401-49-8P 228401-50-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by **raf kinase**)

IT **144378-33-6, Raf Kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by **raf kinase**)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:776672 HCAPLUS
DN 130:38284
TI Preparation of urea derivatives as **raf kinase** inhibitors
IN **Wood, Jill E.**; Wild, Hanno; Rogers, Daniel H.; Lyons, John; Katz, Michael E.; Caringal, Yolanda V.; Dally, Robert; Lee, Wendy; **Smith, Roger A.**; Blum, Cheri L.

PA **Bayer** Corp., USA; Onyx Pharmaceuticals; et al.
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9852559 | A1 | 19981126 | WO 1998-US10376 | 19980521 <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9875855 | A1 | 19981211 | AU 1998-75855 | 19980521 <-- |
| | EP 986382 | A1 | 20000322 | EP 1998-923601 | 19980521 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 2002500650 | T2 | 20020108 | JP 1998-550618 | 19980521 <-- |
| PRAI | US 1997-863021 | A2 | 19970523 <-- | | |
| | WO 1998-US10376 | W | 19980521 | | |

AB Substituted urea compds., useful for treating tumors mediated by **raf kinase** (no data), were prepd. E.g., reaction of Me thioglycolate and 3-chloro-4-methyl-2-pentenenitrile gave 16% of the 3-aminothiophene deriv., which was reacted with 4-MeC6H4NCO to give Me 5-isopropyl-3-(3-p-tolylureido)thiophene-2-carboxylate.

IT **216573-01-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of urea derivs. as **raf kinase** inhibitors)

IT **216573-03-4P 216573-34-1P 216574-09-3P**
**216574-10-6P 216574-11-7P 216589-05-8P**
**216589-46-7P 216852-73-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea derivs. as **raf kinase** inhibitors)

IT **149719-32-4, v-Raf kinase**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of urea derivs. as **raf kinase** inhibitors)

IT **216591-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of urea derivs. as **raf kinase** inhibitors)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l46 bib abs hitrn tot

L46 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:746592 HCAPLUS
DN 136:95577
TI Discovery of heterocyclic ureas as a new class of **raf kinase** inhibitors: identification of a second generation lead by a combinatorial chemistry approach
AU **Smith, R. A.**; Barbosa, J.; Blum, C. L.; Bobko, M. A.; Caringal,

Y. V.; Dally, R.; Johnson, J. S.; Katz, M. E.; Kennure, N.; Kingery-Wood, J.; Lee, W.; **Lowinger, T. B.**; Lyons, J.; Marsh, V.; Rogers, D. H.; Swartz, S.; Walling, T.; Wild, H.

CS Department of Chemistry Research, **Bayer** Research Center, West Haven, CT, 06516, USA

SO Bioorganic & Medicinal Chemistry Letters (2001), 11(20), 2775-2778
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science Ltd.

DT Journal

LA English

AB Heterocyclic ureas, such as N-3-thienyl N'-aryl ureas, have been identified as novel inhibitors of **raf kinase**, a key mediator in the ras signal transduction pathway. Structure-activity relationships were established, and the potency of the screening hit was improved 10-fold to IC50=1.7 .mu.M. A combinatorial synthesis approach enabled the identification of a breakthrough lead (IC50=0.54 .mu.M) for a second generation series of heterocyclic urea **raf kinase** inhibitors.

IT **144378-33-6, Raf kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heterocyclic ureas as **raf kinase** inhibitors)

IT **216572-95-1P 216573-01-2P 216573-03-4P**
**216573-09-0P 216573-13-6P 216573-17-0P**
**216573-24-9P 216573-25-0P 216573-26-1P**
**216573-27-2P 216573-34-1P 216574-41-3P**
**216574-53-7P 216589-05-8P 216589-46-7P**
**216591-27-4P 229003-21-8P 329260-25-5P**
**329260-39-1P 329260-45-9P 329260-47-1P**
**329260-78-8P 329260-80-2P 329260-82-4P**
**329260-84-6P 371974-26-4P 389069-17-4P**
**389069-18-5P 389069-19-6P 389069-20-9P**
**389069-21-0P 389069-22-1P 389070-11-5P**
**389070-12-6P 389070-13-7P 389070-14-8P**
**389070-15-9P 389070-21-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclic ureas as **raf kinase** inhibitors)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:493516 HCAPLUS

DN 133:120157

TI Preparation of .omega.-carboxy(hetero)aryl substituted diphenyl ureas as **raf kinase** inhibitors

IN **Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.**; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PA **Bayer** Corporation, USA

SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000042012 | A1 | 20000720 | WO 2000-US648 | 20000112 |

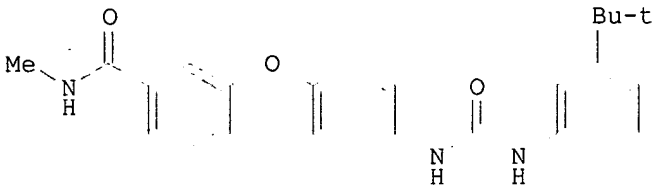
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| EP 1140840 | A1 | 20011010 | EP 2000-903239 | 20000112 | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| US 2001011135 | A1 | 20010802 | US 2001-773659 | 20010202 | |
| US 2001011136 | A1 | 20010802 | US 2001-773675 | 20010202 | |
| US 2001016659 | A1 | 20010823 | US 2001-773672 | 20010202 | |
| US 2001027202 | A1 | 20011004 | US 2001-773658 | 20010202 | |
| US 2001034447 | A1 | 20011025 | US 2001-773604 | 20010202 | |
| NO 2001003463 | A | 20010912 | NO 2001-3463 | 20010712 | |
| US 2002042517 | A1 | 20020411 | US 2001-948915 | 20010910 | |
| PRAI US 1999-115877P | P | 19990113 | | | |
| US 1999-257266 | A2 | 19990225 | | | |
| US 1999-425228 | A2 | 19991022 | | | |
| WO 2000-US648 | W | 20000112 | | | |

OS MARPAT 133:120157

GI




II

AB This invention relates to the prepn. and use of (hetero)aryl ureas ANHCONHB [I; A = L(ML1)q; L = 5- or 6-membered (hetero)aryl, esp. Ph or pyridinyl; M = bridging group; L1 = (hetero)aryl with at least one (un)substituted sulfamoyl, carboxy, or carbamoyl substituent; q = 1-3; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] for the treatment of raf mediated diseases, such as cancer (no data). Approx. 100 invention compds. and numerous intermediates were prepd. For instance, 3-tert-butylaniline was coupled with bis(trichloromethyl)carbonate to form the isocyanate, followed by addn. of 4-(3-N-methylcarbamoylphenoxy)aniline (prepn. given) to afford the urea II.

IT **284461-33-2P**, N-(3-tert-Butylphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl)urea **284461-34-3P**, N-(3-tert-Butylphenyl)-N'-(4-(4-acetylphenoxy)phenyl)urea **284461-36-5P**, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea **284461-37-6P**, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl]urea **284461-39-8P**, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1-oxoisoindolin-5-yloxy)phenyl]urea **284461-42-3P 284461-43-4P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284461-44-5P 284461-45-6P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284461-51-4P 284461-54-7P 284461-58-1P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[[2-(N-methylcarbamoyl)-4-pyridyl]thio]phenyl]urea **284461-74-1P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284461-75-2P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284461-78-5P 284461-86-5P 284461-90-1P**

**284461-99-0P 284462-05-1P 284462-06-2P**
**284462-17-5P 284462-18-6P 284462-19-7P,**
N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[2-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-20-0P,**
N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-22-2P,**
N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-26-6P 284462-28-8P,**
N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-30-2P**
**284462-31-3P,** N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-35-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea **raf kinase** inhibitors by reacting arylisocyanates with arylamines)

IT **228418-48-2P 284461-35-4P 284461-40-1P**
**284461-41-2P 284461-46-7P 284461-47-8P**
**284461-49-0P 284461-50-3P 284461-52-5P**
**284461-53-6P 284461-55-8P 284461-56-9P**
**284461-57-0P 284461-59-2P 284461-60-5P**
**284461-61-6P 284461-62-7P 284461-63-8P**
**284461-64-9P 284461-65-0P 284461-66-1P**
**284461-67-2P 284461-68-3P 284461-69-4P**
**284461-70-7P 284461-71-8P 284461-72-9P**
**284461-77-4P 284461-79-6P 284461-80-9P**
**284461-81-0P 284461-82-1P 284461-83-2P**
**284461-84-3P 284461-85-4P 284461-88-7P**
**284461-91-2P 284461-92-3P 284461-93-4P**
**284461-94-5P 284461-95-6P 284461-96-7P**
**284461-97-8P 284461-98-9P 284462-00-6P**
**284462-01-7P 284462-02-8P 284462-03-9P**
**284462-04-0P 284462-07-3P 284462-08-4P**
**284462-09-5P 284462-10-8P 284462-11-9P**
**284462-12-0P 284462-13-1P 284462-15-3P**
**284462-16-4P 284462-21-1P 284462-23-3P**
**284462-24-4P 284462-25-5P 284462-27-7P**
**284462-32-4P 284462-33-5P 284462-34-6P**
**284462-36-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea **raf kinase** inhibitors by reacting arylisocyanates with arylamines)

IT **284461-38-7,** N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1,3-dioxoisoindolin-5-yloxy)phenyl]urea **284461-48-9**
**284461-76-3,** N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-((2-(N-Methylcarbamoyl)-4-pyridyl)oxy)phenyl)urea **284462-29-9**
**284462-76-6 284671-00-7,** N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea
**284671-01-8,** N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-(3-carboxyphenyl)urea
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea **raf kinase** inhibitors by reacting arylisocyanates with arylamines)

IT **284461-73-0P 284461-89-8P 284462-67-5P,**
N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'(4-aminophenyl)Urea
**284462-68-6P,** N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'(4-

ethoxycarbonylphenyl)Urea **284462-69-7P 284462-70-0P**
**284462-71-1P 284462-97-1P 284670-98-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea **raf kinase** inhibitors by reacting arylisocyanates with arylamines)
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil reg
FILE 'REGISTRY' ENTERED AT 11:16:56 ON 02 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES: 30 APR 2002 HIGHEST RN 409303-45-3
DICTIONARY FILE UPDATES: 30 APR 2002 HIGHEST RN 409303-45-3

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d his l47-

(FILE 'HCAPLUS' ENTERED AT 11:04:15 ON 02 MAY 2002)

FILE 'REGISTRY' ENTERED AT 11:14:47 ON 02 MAY 2002

FILE 'HCAPLUS' ENTERED AT 11:15:08 ON 02 MAY 2002
SEL HIT RN L44

FILE 'REGISTRY' ENTERED AT 11:16:11 ON 02 MAY 2002
L47 332 S E1-E332
L48 2 S L47 AND L6,L12
L49 330 S L47 NOT L48

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=> d ide can tot l48

L48 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN **149719-32-4** REGISTRY
CN Kinase (phosphorylating), gene v-raf protein (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Gene v-raf kinase**
CN Gene v-raf serine-threonine protein kinase
CN **v-Raf kinase**
CN v-Raf serine/threonine kinase
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
10 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:41379

REFERENCE 2: 130:38284

REFERENCE 3: 126:262519

REFERENCE 4: 126:142645

REFERENCE 5: 124:6073

REFERENCE 6: 122:6851

REFERENCE 7: 121:131197

REFERENCE 8: 119:244070

REFERENCE 9: 119:154375

REFERENCE 10: 119:153266

L48 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN **144378-33-6** REGISTRY
CN Kinase (phosphorylating), gene c-raf protein (9CI) (CA INDEX NAME)
OTHER NAMES:
CN C-raf kinase
CN Gene c-Raf protein kinase
CN Gene raf serine/threonine kinase
CN Protein kinase c-Raf
CN Raf kinase
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CIN, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
294 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
297 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:279456

REFERENCE 2: 136:277868

REFERENCE 3: 136:277136

REFERENCE 4: 136:260900

REFERENCE 5: 136:260894

REFERENCE 6: 136:258141

REFERENCE 7: 136:226424

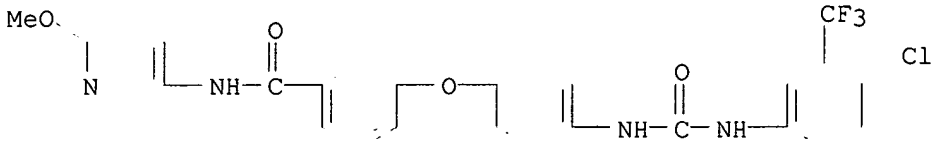
REFERENCE 8: 136:214136

REFERENCE 9: 136:213868

REFERENCE 10: 136:200113

=> d scan l49

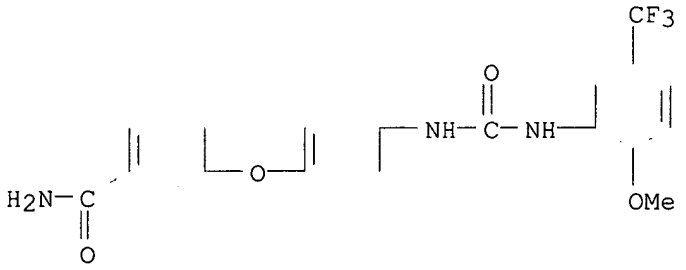
L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amin o]phenoxy]-N-(6-methoxy-3-pyridinyl)- (9CI)
MF C27 H20 Cl F3 N4 O4



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):25

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[4-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]ami no]phenoxy]- (9CI)
MF C22 H18 F3 N3 O4



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
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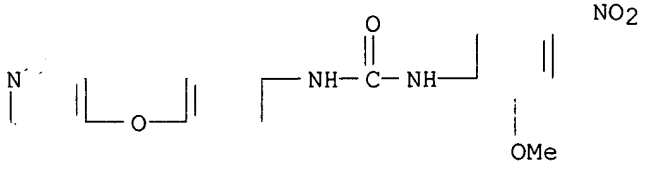
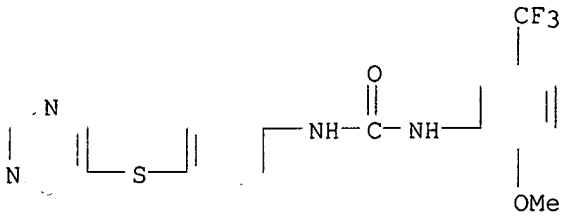
MF C19 H16 N4 O5



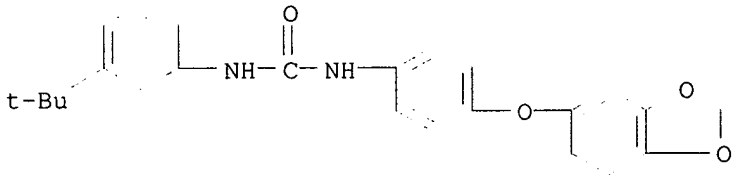
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(5-pyrimidinylthio)phenyl]- (9CI)
MF C19 H15 F3 N4 O2 S



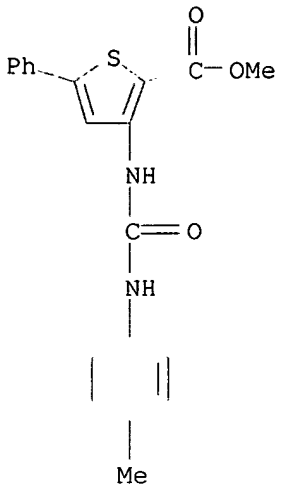
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-(1,3-benzodioxol-5-yloxy)phenyl]-N'-[3-(1,1-dimethylethyl)phenyl]- (9CI)
MF C24 H24 N2 O4



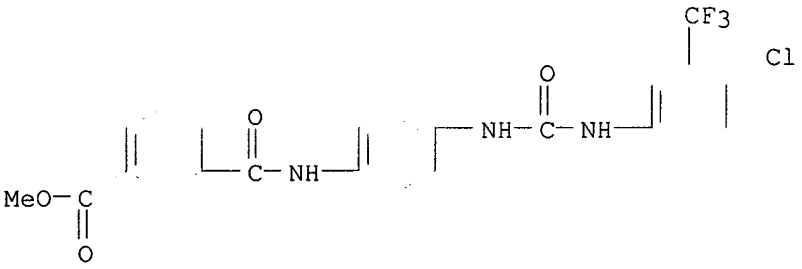
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Thiophenecarboxylic acid, 3-[[[(4-methylphenyl)amino]carbonyl]amino]-5-phenyl-, methyl ester (9CI)
MF C20 H18 N2 O3 S



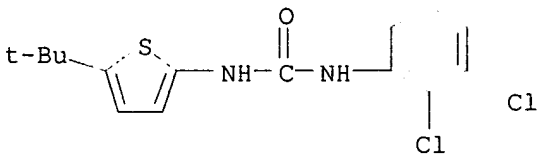
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzoic acid, 3-[[[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl ]amino]phenyl]amino]carbonyl]-, methyl ester (9CI)
MF C23 H17 Cl F3 N3 O4



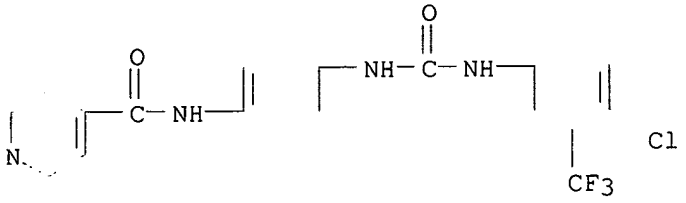
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-(2,3-dichlorophenyl)-N'-[5-(1,1-dimethylethyl)-2-thienyl]- (9CI)
MF C15 H16 Cl2 N2 O S



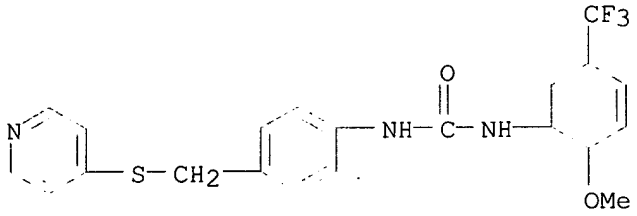
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 4-Pyridinecarboxamide, N-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]- (9CI)
MF C20 H14 Cl F3 N4 O2



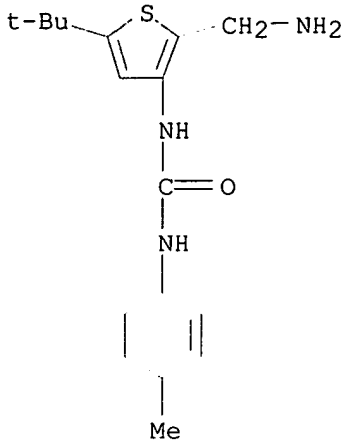
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[(4-pyridinylthio)methyl]phenyl]- (9CI)
MF C21 H18 F3 N3 O2 S



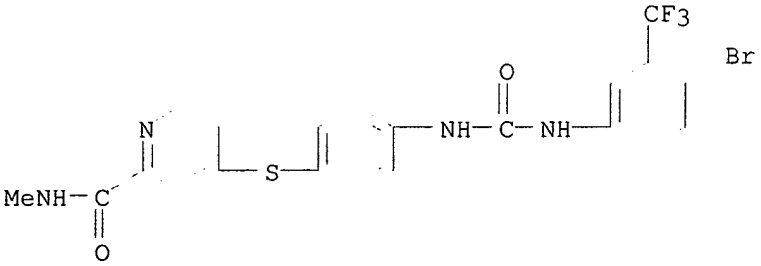
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[2-(aminomethyl)-5-(1,1-dimethylethyl)-3-thienyl]-N'-(4-methylphenyl)- (9CI)
MF C17 H23 N3 O S



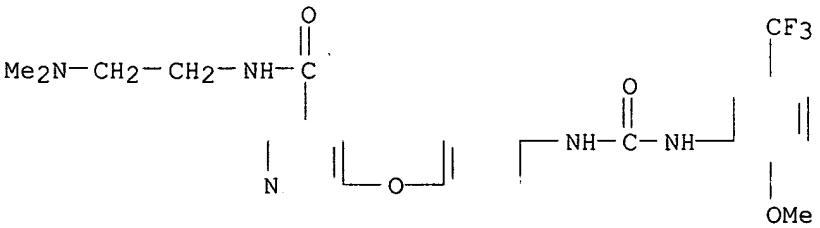
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Pyridinecarboxamide, 4-[[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI)
MF C21 H16 Br F3 N4 O2 S



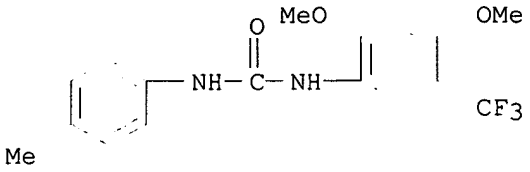
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 3-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-5-[4-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI)
MF C25 H26 F3 N5 O4



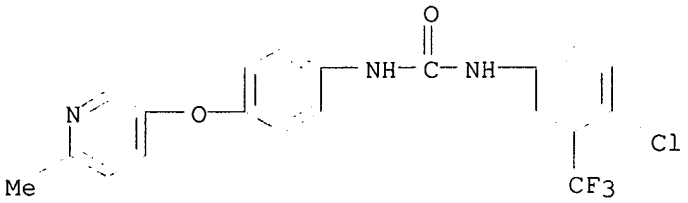
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[2,4-dimethoxy-5-(trifluoromethyl)phenyl]-N'-(4-methylphenyl)-(9CI)
MF C17 H17 F3 N2 O3



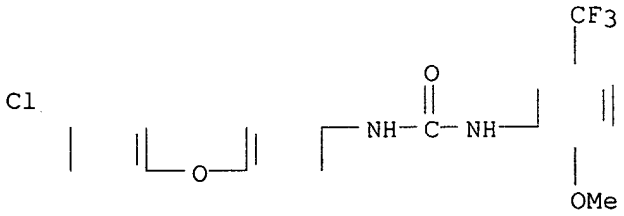

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[(6-methyl-3-pyridinyl)oxy]phenyl]- (9CI)
MF C20 H15 Cl F3 N3 O2



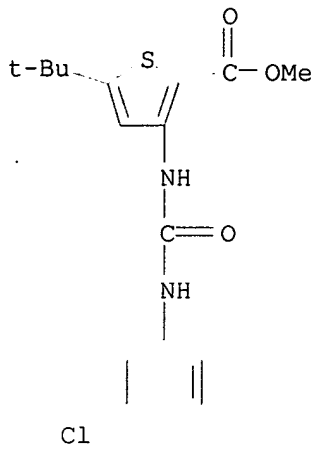

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-(4-chlorophenoxy)phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI)
MF C21 H16 Cl F3 N2 O3



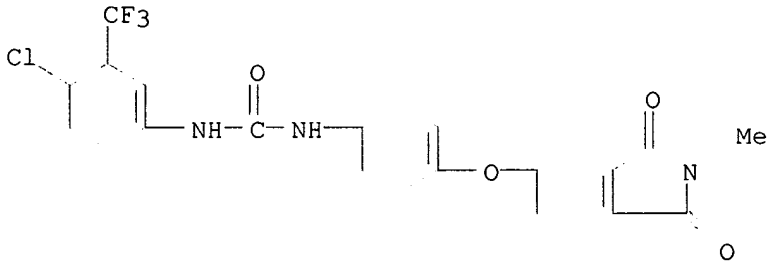

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Thiophenecarboxylic acid, 3-[[[(3-chlorophenyl)amino]carbonyl]amino]-5-(1,1-dimethylethyl)-, methyl ester (9CI)
MF C17 H19 Cl N2 O3 S



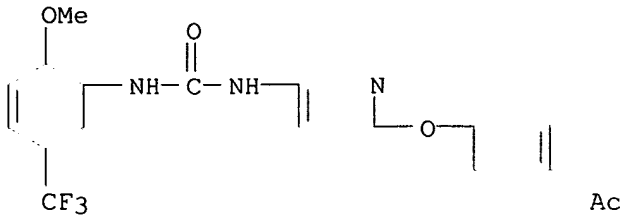
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[(2,3-dihydro-2-methyl-1,3-dioxo-1H-isoindol-5-yl)oxy]phenyl]- (9CI)
MF C23 H15 Cl F3 N3 O4



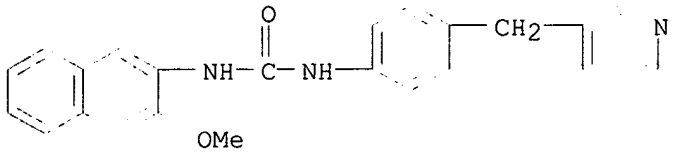
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[6-(4-acetylphenoxy)-3-pyridinyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI)
MF C22 H18 F3 N3 O4



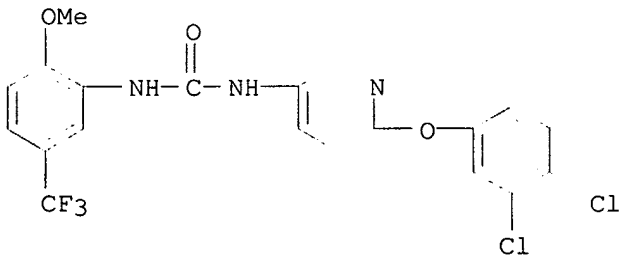
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-(3-methoxy-2-naphthalenyl)-N'-[4-(3-pyridinylmethyl)phenyl]- (9CI)
MF C24 H21 N3 O2



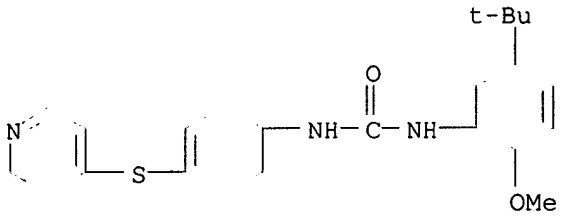
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[6-(3,4-dichlorophenoxy)-3-pyridinyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI)
MF C20 H14 Cl2 F3 N3 O3



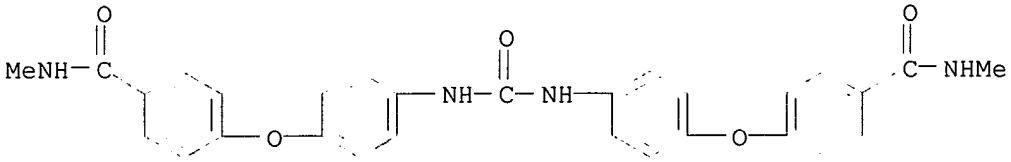
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-(4-pyridinylthio)phenyl]- (9CI)
MF C23 H25 N3 O2 S



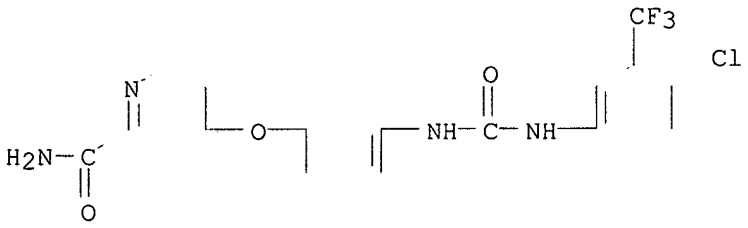
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 4,4'-[carbonylbis(imino-4,1-phenyleneoxy)]bis[N-methyl- (9CI)
MF C29 H26 N4 O5



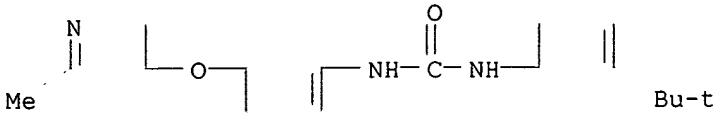
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Pyridinecarboxamide, 4-[3-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI)
MF C20 H14 Cl F3 N4 O3



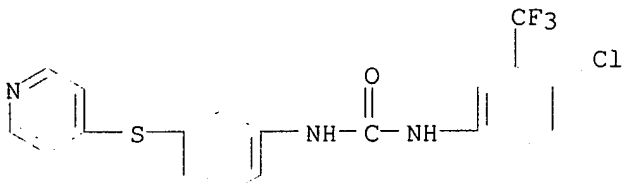
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[3-[(2-methyl-4-pyridinyl)oxy]phenyl]- (9CI)
MF C23 H25 N3 O2
CI COM



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[3-(4-pyridinylthio)phenyl]- (9CI)
MF C19 H13 Cl F3 N3 O S



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> d his l50-

(FILE 'REGISTRY' ENTERED AT 11:16:56 ON 02 MAY 2002)
SAV L49 KUMAR776A/A
L50 23094 S L4 NOT L49

FILE 'HCAPLUS' ENTERED AT 11:17:55 ON 02 MAY 2002
L51 8301 S L50
L52 6940 S L16 AND L51
L53 1728 S L52 AND (1 OR 63)/SC,SX
E ANTITUMOR/CT
E E5+ALL
L54 303 S L52 AND E4,E3+NT

FILE 'HCAPLUS' ENTERED AT 11:38:35 ON 02 MAY 2002
L55 643 S L52 AND (?NEOPLAS? OR ?CANCER? OR ?CARCIN? OR ?TUMOR? OR ?TUM
L56 645 S L54,L55
L57 519 S L53 AND L56
L58 134 S L57 AND P/DT
L59 91 S L58 AND US/PC
L60 44 S L57 AND ?KINASE?
L61 19 S L60 AND L58
L62 1033 S L50 (L) THU/RL
L63 218 S L62 AND L57
L64 97 S L63 AND L58
L65 69 S L64 AND L59
L66 8 S L65 AND L60
L67 19 S L61,L66

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 11:43:30 ON 02 MAY 2002
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 2 May 2002 VOL 136 ISS 18
FILE LAST UPDATED: 30 Apr 2002 (20020430/ED)

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=> d l67 bib abs hitrn fhitstr tot

L67 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:531658 HCAPLUS
DN 133:144896
TI Phosphonated agents and their antiangiogenic and **antitumorigenic** use
IN Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter
PA University of Kentucky Research Foundation, USA
SO U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 899,996, abandoned.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | | APPLICATION NO. | DATE |
|---|---|---|---|---|---|---|
| PI | US 6096730 | A | 20000801 | | US 1998-121124 | 19980723 <-- |
| | US 6160166 | A | 20001212 | | US 1999-357925 | 19990721 <-- |
| PRAI | US 1997-899996 | B2 | 19970724 | <-- | | |
| | US 1998-121124 | A3 | 19980723 | | | |

OS MARPAT 133:144896
AB Phosphonic acid agents are synthesized and characterized which are potent inhibitors of angiogenesis, **tumorigenesis** and metalloproteinase activity. Their method of use for the inhibition of angiogenesis and metalloproteinase and the treatment of **tumors** is also shown.
IT **145-63-1**, Suramin **220239-91-8**, NF 069
**220239-92-9 220239-95-2**, NF 068 **220239-96-3**,
NF 067
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. and pharmaceutical compn. of antiangiogenic and **antitumorigenic** phosphonic acid agents)
IT **111129-57-8P 220240-18-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and pharmaceutical compn. of antiangiogenic and

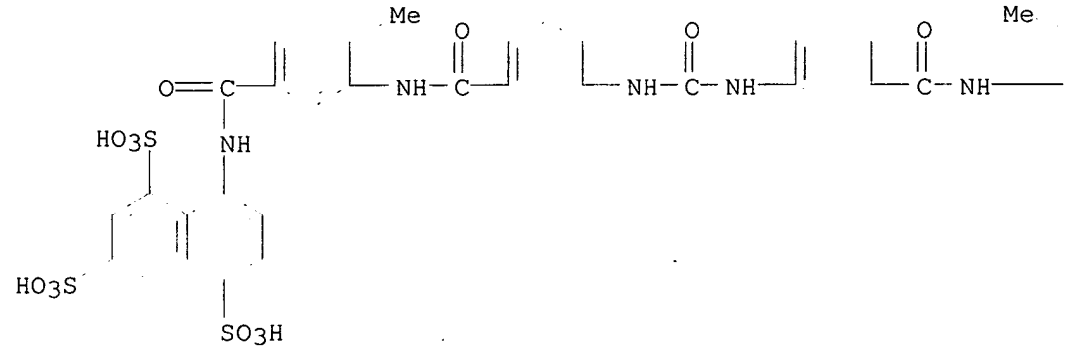
**antitumorigenic** phosphonic acid agents)

IT **145-63-1**, Suramin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. and pharmaceutical compn. of antiangiogenic and **antitumorigenic** phosphonic acid agents)

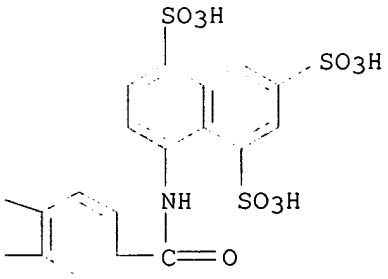
RN 145-63-1 HCAPLUS

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:425745 HCAPLUS

DN 131:87909

TI Inhibition of p38 **kinase** activity using substituted heterocyclic ureas

IN Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko

PA Bayer Corporation, USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9932111 | A1 | 19990701 | WO 1998-US26080 | 19981222 <-- |
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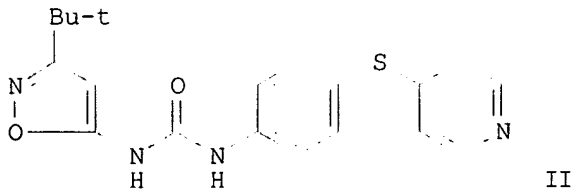
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2315720 | AA | 19990701 | CA 1998-2315720 | 19981222 <-- |
| | AU 9919971 | A1 | 19990712 | AU 1999-19971 | 19981222 <-- |
| | AU 739642 | B2 | 20011018 | | |
| | EP 1041982 | A1 | 20001011 | EP 1998-964709 | 19981222 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | JP 2001526223 | T2 | 20011218 | JP 2000-525102 | 19981222 <-- |
| PRAI | US 1997-995750 | A | 19971222 <-- | | |
| | WO 1998-US26080 | W | 19981222 | | |

OS MARPAT 131:87909
GI




II

AB A method for treatment of p38-mediated disease other than **cancer** comprises administration of ANHCONHB [I; A = substituted isoxazolyl, pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. .gtoreq.1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-(4-pyridinylthio)aniline with 3-tert-butyl-5-isoxazolyl isocyanate in toluene gave title compd. II. In an in vitro p38 **kinase** assay, I displayed IC50 values of 1-10 .mu.M.

IT **229003-12-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

IT **229002-65-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

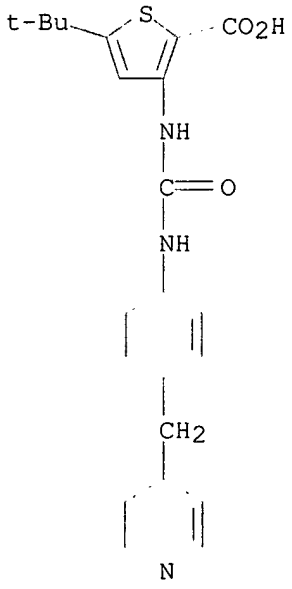
IT **227623-30-5P 227623-31-6P 229002-62-4P 229002-63-5P 229002-66-8P 229002-67-9P 229002-70-4P 229002-72-6P 229002-74-8P**

**229002-76-0P 229002-93-1P 229002-95-3P**
**229002-96-4P 229155-57-1P 229155-58-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

IT **229003-21-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

IT **229003-12-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

RN 229003-12-7 HCAPLUS
CN 2-Thiophenecarboxylic acid, 5-(1,1-dimethylethyl)-3-[[[[4-(4-pyridinylmethyl)phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)




RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:421667 HCAPLUS
DN 131:58659
TI Preparation of diaryl ureas as inhibitors of p38 **kinase**.
IN Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Hatoum-Mokdad, Holia; Rodriguez, Mareli; Sibley, Robert; Wang, Ming
PA Bayer Corporation, USA
SO PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

PI WO 9932463 A1 19990701 WO 1998-US27265 19981222 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2315715 AA 19990701 CA 1998-2315715 19981222 <--
AU 9919399 A1 19990712 AU 1999-19399 19981222 <--
EP 1042305 A1 20001011 EP 1998-964221 19981222 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2001526276 T2 20011218 JP 2000-525400 19981222 <--
PRAI US 1997-995749 A 19971222 <--
WO 1998-US27265 W 19981222
OS MARPAT 131:58659
AB A method of treating a p-38 mediated disease other than **cancer** comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl contg. .gtoreq.1 6-membered arom. structure contg. 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuranyloxy)aniline (prepn. given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 **kinase** with IC50 = 1-10 .mu.M.
IT **228416-78-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diaryl ureas as inhibitors of p38 **kinase**)
IT **370-50-3P 117745-34-3P 228399-32-4P**
**228399-33-5P 228399-34-6P 228399-35-7P**
**228399-38-0P 228399-44-8P 228399-45-9P**
**228399-61-9P 228399-62-0P 228399-63-1P**
**228399-65-3P 228399-66-4P 228399-68-6P**
**228399-69-7P 228399-70-0P 228399-71-1P**
**228399-72-2P 228399-74-4P 228399-82-4P**
**228399-84-6P 228400-63-3P 228400-64-4P**
**228400-65-5P 228400-87-1P 228400-92-8P**
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**228401-00-1P 228401-01-2P 228401-02-3P**
**228401-03-4P 228401-04-5P 228401-07-8P**
**228416-61-3P 228416-62-4P 228416-63-5P**
**228416-64-6P 228416-65-7P 228416-66-8P**
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**228416-73-7P 228416-74-8P 228416-75-9P**
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**228417-97-8P 228417-98-9P 228417-99-0P**
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**228418-03-9P 228418-04-0P 228418-05-1P**
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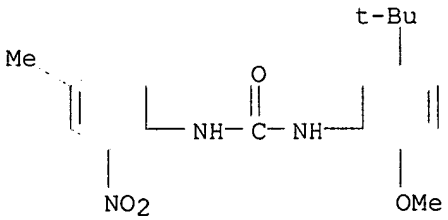
**228418-42-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diaryl ureas as inhibitors of p38 **kinase**)

IT **228399-41-5 228418-48-2 228418-49-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of diaryl ureas as inhibitors of p38 **kinase**)

IT **228416-78-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diaryl ureas as inhibitors of p38 **kinase**)

RN 228416-78-2 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-(4-methyl-2-nitrophenyl)- (9CI) (CA INDEX NAME)



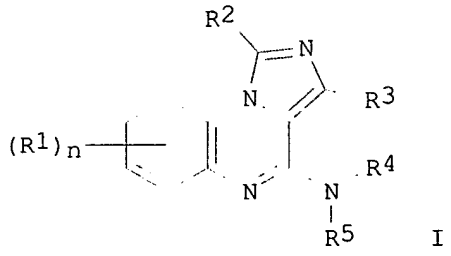

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:166498 HCAPLUS
DN 130:223295
TI Preparation of imidazoquinoxaline protein tyrosine **kinase** inhibitors

IN Barrish, Joel C.; Chen, Ping; Das, Jagabandhu; Iwanowicz, Edwin J.; Norris, Derek J.; Padmanabha, Ramesh; Roberge, Jacques Y.; Schieven, Gary L.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 315 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9909845 | A1 | 19990304 | WO 1998-US16027 | 19980803 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6235740 | B1 | 20010522 | US 1998-97338 | 19980615 <-- |
| AU 9886817 | A1 | 19990316 | AU 1998-86817 | 19980803 <-- |

PRAI US 1997-56770P P 19970825 <--
US 1997-69159P P 19971209 <--
WO 1998-US16027 W 19980803
OS MARPAT 130:223295
GI

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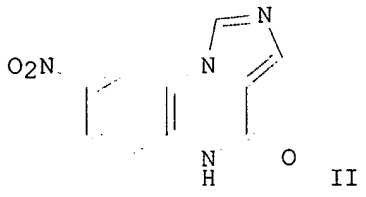
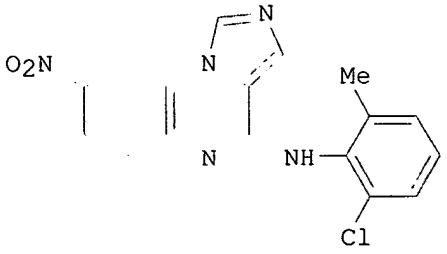



II




III

AB Novel imidazoquinoxalines I and salts thereof are disclosed [wherein: n = 0-4; R1, R2, R3 = H, R6, OH, OR6, SH, SR6, CO2H, SO3H, halo, cyano, NO2, etc.; R1-R3 may form ring(s); R4, R5 = H, R6, COR6; or NR4R5 forms (un)substituted 3- to 8-membered heterocyclic ring; R6 = (un)substituted alk(en/yn)yl, cycloalk(en)yl(alkyl), aryl, aralkyl, heterocyclo(alkyl)]. Also disclosed are pharmaceutical compns. contg. the compds., and methods of their use in the treatment of various protein tyrosine **kinase** -assocd. disorders, such as immunol. disorders (no data). Over 500 synthetic examples are given. For instance, the

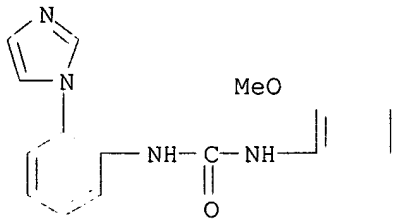
nitroimidazoloquinoxalinone II (prepd. in 4 steps) was treated with POCl3 to give 78% of the corresponding chloro compd., which reacted with NaN(SiMe3)2 and 2-chloro-6-methylaniline in THF to give 86% title compd. III.

IT **68008-32-2P 221068-10-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; prepn. of imidazoquinoxalines as protein tyrosine **kinase** inhibitors)

IT **68008-32-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; prepn. of imidazoquinoxalines as protein tyrosine **kinase** inhibitors)

RN 68008-32-2 HCAPLUS

CN Urea, N-[2-(1H-imidazol-1-yl)phenyl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)




RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:96248 HCAPLUS

DN 130:148689

TI Phosphonated agents and their antiangiogenic and **antitumorigenic** use

IN Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter

PA University of Kentucky Research Foundation, USA

SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9905148 | A1 | 19990204 | WO 1998-US15470 | 19980724 <-- |
| | W: AU, CA, JP, MX | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | AU 9885915 | A1 | 19990216 | AU 1998-85915 | 19980724 <-- |
| | AU 739637 | B2 | 20011018 | | |
| | EP 1019419 | A1 | 20000719 | EP 1998-937133 | 19980724 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| PRAI | US 1997-899996 | A | 19970724 <-- | | |
| | WO 1998-US15470 | W | 19980724 | | |

OS MARPAT 130:148689

AB The present invention relates to novel phosphonic acid substituted agents and their pharmaceutical compns. Phosphonic acid substituted agents that are potent inhibitors of angiogenesis or **tumorigenesis** is defined by the following formula: (P-Yn1)m1-Q1-K-(Q2-(Yn2-P)m2)j (P = phosphonic group, phosphonic salt; Y = OCO, NR1CO, CON(R1)R2; Q1, Q2 = aryl; K = H, NHCONH, NHCSNH, NHCOR3, NHCSR3CSNH; j, n1, n2 = 0-2; m1, m2 = 1-4; R1 = H, CH2CO2H, alkyl; R2 = alkyl, aryl, alkaryl; R3 = aryl). A

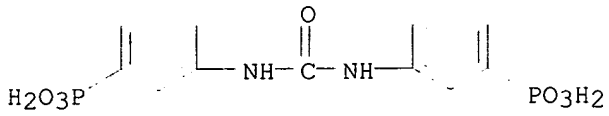
pharmaceutical compn. for the treatment of angiogenesis-dependent conditions or **tumors** comprises an effective amt. of a phosphonic acid agent and a pharmaceutically acceptable carrier. Some of the phosphonic acid agents were more potent inhibitors of angiogenesis in the chick chorioallantoic membrane (CAM) assay and to human microvascular endothelial cell growth than suramin.

IT **220240-08-4P 220240-09-5P 220240-14-2P**
**220240-16-4P 220240-17-5P 220240-18-6P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphonic acid agents and their antiangiogenic and **antitumorigenic** use)

IT **220239-81-6 220239-82-7 220239-83-8**
**220239-84-9 220239-85-0 220239-86-1**
**220239-87-2 220239-88-3 220239-89-4**
**220239-90-7 220239-91-8 220239-92-9**
**220239-95-2 220239-96-3 220239-97-4**
**220239-98-5 220240-02-8 220240-03-9**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphonic acid agents and their antiangiogenic and **antitumorigenic** use)

IT **220240-08-4P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphonic acid agents and their antiangiogenic and **antitumorigenic** use)

RN 220240-08-4 HCAPLUS
CN Phosphonic acid, [carbonylbis(imino-3,1-phenylene)]bis- (9CI) (CA INDEX NAME)




RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:34888 HCAPLUS
DN 130:66491
TI Preparation of urea derivatives as inhibitors of p38
IN Salituro, Francesco Gerald; Bemis, Guy W.; Green, Jeremy; Kofron, James L.
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9900357 | A1 | 19990107 | WO 1998-US13496 | 19980629 <-- |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6093742 A 20000725 US 1997-884160 19970627 <--
AU 9883776 A1 19990119 AU 1998-83776 19980629 <--
EP 993441 A1 20000419 EP 1998-934195 19980629 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI US 1997-884160 A 19970627 <--
WO 1998-US13496 W 19980629

OS MARPAT 130:66491

AB The title compds. WX1C(:Y)X2Z [W = (un)substituted satd., partially satd. or arom. monocyclic or bicyclic ring system optionally comprising up to 4 heteroatoms; Y = O, etc.; X1, X2 = O, S, etc.; Z = cycloalkyl, etc.] are prepd. Compds. of this invention are inhibitors of p38, a mammalian protein **kinase** involved in cell **proliferation**, cell death and response to extracellular stimuli. In in vitro assays for inhibition of phosphorylation of EGF receptor peptide, compds. of this invention showed IC50 values of 0.14 .mu.M to 19 .mu.M.

IT **101-20-2P 369-81-3P 1566-96-7P**
**2008-73-3P 4300-43-0P 13114-79-9P**
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**13142-48-8P 13142-50-2P 13143-23-2P**
**13208-22-5P 13256-73-0P 16655-20-2P**
**85260-98-6P 107917-67-9P 117745-34-3P**
**196617-12-6P 196617-13-7P 196700-19-3P**
**196700-39-7P 196700-55-7P 196700-64-8P**
**197800-69-4P 199741-56-5P 202598-90-1P**
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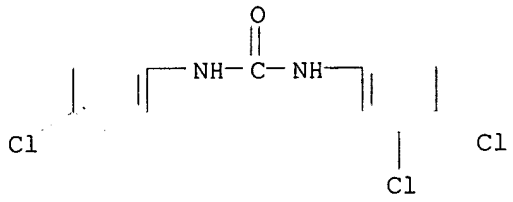
**218136-15-3P 218136-17-5P 218136-18-6P**
**218136-19-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic**

**use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea derivs. as inhibitors of p38)

IT **101-20-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea derivs. as inhibitors of p38)

RN 101-20-2 HCAPLUS
CN Urea, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:776671 HCAPLUS
DN 130:38286
TI Inhibition of p38 **kinase** activity by aryl ureas
IN Ranges, Gerald; Scott, William; Bombara, Michael; Rauner, Deborah; Redman, Aniko; Smith, Roger; Paulsen, Holger; Chen, Jinshan; Gunn, David; Renick, Joel
PA Bayer Corp., USA; et al.
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | | APPLICATION NO. | DATE | |
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| PI | WO 9852558 | A1 | 19981126 | | WO 1998-US10375 | 19980521 | <-- |
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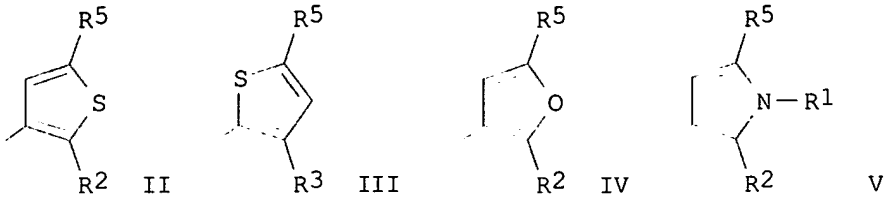
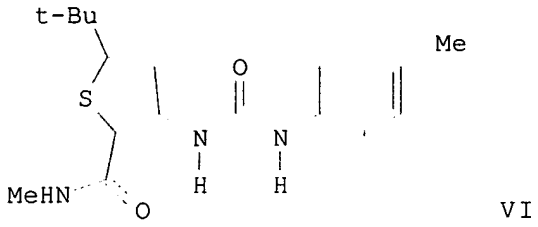
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | | | |
| | AU 9875854 | A1 | 19981211 | | AU 1998-75854 | 19980521 | <-- |
| | EP 1019040 | A1 | 20000719 | | EP 1998-923600 | 19980521 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | | | |
| | JP 2001526687 | T2 | 20011218 | | JP 1998-550617 | 19980521 | <-- |
| | US 6344476 | B1 | 20020205 | | US 1998-83396 | 19980522 | <-- |
| PRAI | US 1997-863022 | A2 | 19970523 | <-- | | | |
| | US 1997-98557P | P | 19970523 | <-- | | | |
| | WO 1998-US10375 | W | 19980521 | | | | |

OS MARPAT 130:38286
GI



II III IV V



VI

AB The title ureas ANHC(O)NHB [I; A = (un)substituted C6-12 aryl, C5-12 heteroaryl; B = II-V; R1 = H, C1-4 alkyl; R2, R3 = halo, COOR1, CN, etc.; R5 = C3-5 alkyl], useful in treating cytokine mediated diseases other than **cancer** and proteolytic enzyme mediated diseases other than **cancer**, were prepd. Thus, reaction of N-methyl-3-amino-5-tert-butylthiophene-2-carboxamide (prepn. given) with 4-methylphenyl isocyanate in PhMe afforded 44% the title compd. VI. Compds. I are useful in treating diseases mediated by TNF.alpha., MMP-1, MMP-3, IL-1, IL-6, or IL-8 such as rheumatoid arthritis, osteoporosis, asthma, septic shock, inflammatory bowel disease, or the result of host-vs.-graft reactions. All exemplified compds. I showed p38 IC50s of 1 nM - 10 .mu.M.

IT **216573-01-2P 216574-43-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibition of p38 **kinase** activity by aryl ureas)

IT **216572-93-9P 216572-95-1P 216572-97-3P**
**216572-99-5P 216573-03-4P 216573-05-6P**
**216573-07-8P 216573-09-0P 216573-11-4P**
**216573-13-6P 216573-15-8P 216573-16-9P**
**216573-17-0P 216573-21-6P 216573-22-7P**
**216573-23-8P 216573-24-9P 216573-25-0P**
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**216573-35-2P 216573-36-3P 216573-37-4P**
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**216574-12-8P 216574-13-9P 216574-14-0P**
**216574-15-1P 216574-16-2P 216574-17-3P**
**216574-18-4P 216574-19-5P 216574-20-8P**
**216574-21-9P 216574-22-0P 216574-23-1P**
**216574-24-2P 216574-25-3P 216574-26-4P**
**216574-27-5P 216574-28-6P 216574-29-7P**
**216574-30-0P 216574-31-1P 216574-32-2P**

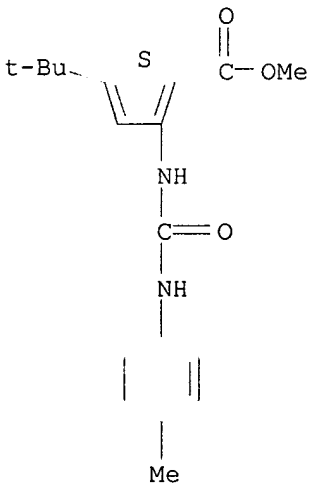
**216574-33-3P 216574-34-4P 216574-35-5P**
**216574-36-6P 216574-37-7P 216574-38-8P**
**216574-39-9P 216574-40-2P 216574-41-3P**
**216574-42-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibition of p38 **kinase** activity by aryl ureas)

IT **216574-76-4 216574-77-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(inhibition of p38 **kinase** activity by aryl ureas)

IT **216574-53-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(inhibition of p38 **kinase** activity by aryl ureas)

IT **216573-01-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibition of p38 **kinase** activity by aryl ureas)

RN 216573-01-2 HCAPLUS
CN 2-Thiophenecarboxylic acid, 5-(1,1-dimethylethyl)-3-[[[(4-methylphenyl)amino]carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)




RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:352627 HCAPLUS
DN 129:54476
TI Protein **kinase** inhibitors for treatment of neurological disorders
IN Lewis, Michael E.; Kauer, James C.; Neff, Nicola; Roberts-Lewis, Jill; Murakata, Chikara; Saito, Hiromitsu; Matsuda, Yuzuru; Glicksman, Marcie A.; Kanai, Fumihiko; Kaneko, Masami
PA Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SO U.S., 61 pp. Cont.-in-part of U.S. Ser. No. 329,540.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 6

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| | | | | | | |
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| PI | US 5756494 | A | 19980526 | US 1995-456642 | 19950602 | <-- |
| | US 5461146 | A | 19951024 | US 1993-96561 | 19930722 | <-- |
| | EP 768312 | A2 | 19970416 | EP 1996-116661 | 19930726 | <-- |
| | EP 768312 | A3 | 19970604 | | | |
| | EP 768312 | B1 | 20000906 | | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | | |
| | EP 1002534 | A1 | 20000524 | EP 1999-120008 | 19930726 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | | |
| | US 5621100 | A | 19970415 | US 1994-329540 | 19941026 | <-- |
| | CA 2203767 | AA | 19960509 | CA 1995-2203767 | 19951004 | <-- |
| | WO 9613506 | A1 | 19960509 | WO 1995-US12965 | 19951004 | <-- |
| | W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | | |
| | RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | | |
| | AU 9539516 | A1 | 19960523 | AU 1995-39516 | 19951004 | <-- |
| | AU 704314 | B2 | 19990422 | | | |
| | EP 788501 | A1 | 19970813 | EP 1995-937391 | 19951004 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| | BR 9509480 | A | 19970930 | BR 1995-9480 | 19951004 | <-- |
| | JP 10510514 | T2 | 19981013 | JP 1995-514605 | 19951004 | <-- |
| | EP 1125938 | A1 | 20010822 | EP 2001-110483 | 19951004 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV | | | | | |
| | US 5741808 | A | 19980421 | US 1997-800383 | 19970214 | <-- |
| PRAI | US 1992-920102 | B2 | 19920724 | <-- | | |
| | US 1993-96561 | A2 | 19930722 | <-- | | |
| | US 1994-329540 | A2 | 19941026 | <-- | | |
| | EP 1993-917337 | A3 | 19930726 | <-- | | |
| | EP 1996-116661 | A3 | 19930726 | <-- | | |
| | US 1995-456642 | A | 19950602 | <-- | | |
| | EP 1995-937391 | A3 | 19951004 | <-- | | |
| | WO 1995-US12965 | W | 19951004 | <-- | | |

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Derivs. of K-252a I (R = HO, MeO; R1 = H, Br, NHCONHPh, CH2SPh, 2-pyrimidinylthiomethyl, 2-furylmethylthiomethyl, etc.; R2 = H, Br, Cl, CH2OH, etc.; R 3 = CH2OH, CO2Me, CH2NHCO2Ph, CONHPh, CH2NHCO2Me, etc.; Z = O, H2), as well as novel bis-N-substituted derivs. of staurosporine XNMeWNMeX (W = C(:Y)NH, W1NHC(:Y); W1 = hydrocarbylene radical of 2-20 carbon atoms; Y = O, S) were prepd. The invention also features a method for treating diseased neuronal cells involving the administration of either the novel staurosporine derivs. or specified functional derivs. of K-252a. Thus, staurosporine was treated with hexamethyl-bis-isocyanate to give 1,6-hexamethylene-bis-(carbamylstaurosporine). The spinal cord choline acetyltransferase (CHAT) activity of I (R = OH, R1 = R2 = Br; R3 = CH2OH, Z = H2) at 300 nM was 146 compared with K-252a of 100.

IT **121664-76-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of staurosporine and K-252a derivs. as protein **kinase** inhibitors for treatment of neurol. disorders)

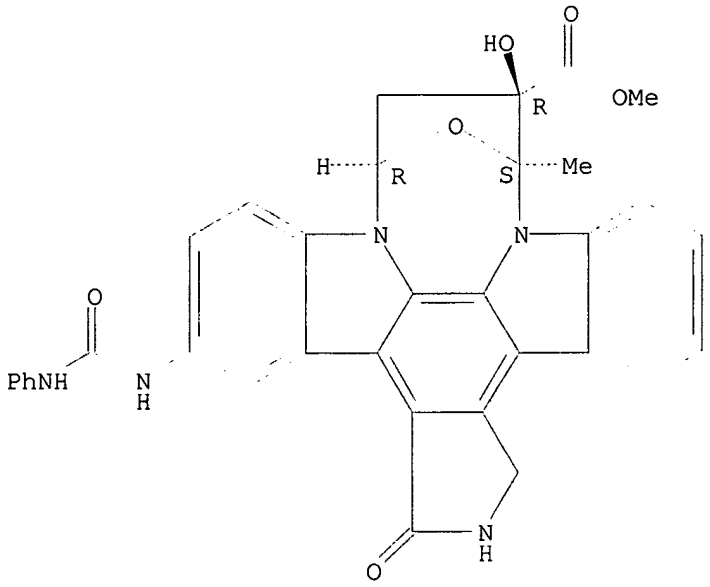
IT **121664-76-4P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of staurosporine and K-252a derivs. as protein **kinase** inhibitors for treatment of neurol. disorders)

RN 121664-76-4 HCAPLUS

CN 9,12-Epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-9-methyl-1-oxo-16-[[(phenylamino)carbonyl]amino]-, methyl ester, (9S,10R,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L67 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:202672 HCAPLUS

DN 128:257439

TI Preparation of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine **kinase** mediated cellular **proliferation**

IN Blankley, Clifton John; Doherty, Annette Marian; Hamby, James Marino; Panek, Robert Lee; Schroeder, Mel Conrad; Showalter, Howard Daniel Hollis; Connolly, Cleo

PA USA

SO U.S., 36 pp. Cont.-in-part of U.S. Ser. No. 339,051, abandoned.
CODEN: USXXAM

DT **Patent**

LA English

FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 5733913 | A | 19980331 | US 1995-539410 | 19951106 <-- |
| CA 2199964 | AA | 19960523 | CA 1995-2199964 | 19951113 <-- |
| WO 9615128 | A2 | 19960523 | WO 1995-US14700 | 19951113 <-- |
| W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9641078 | A1 | 19960606 | AU 1996-41078 | 19951113 <-- |
| AU 711426 | B2 | 19991014 | | |
| EP 790997 | A2 | 19970827 | EP 1995-939129 | 19951113 <-- |

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| | EP 790997 | B1 | 20000322 | | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| | HU 76853 | A2 | 19971229 | HU 1997-1511 | 19951113 | <-- |
| | CN 1169726 | A | 19980107 | CN 1995-196230 | 19951113 | <-- |
| | JP 10509452 | T2 | 19980914 | JP 1995-516240 | 19951113 | <-- |
| | CZ 286160 | B6 | 20000112 | CZ 1997-1390 | 19951113 | <-- |
| | AT 190978 | E | 20000415 | AT 1995-939129 | 19951113 | <-- |
| | ES 2146782 | T3 | 20000816 | ES 1995-939129 | 19951113 | <-- |
| | SK 281724 | B6 | 20010710 | SK 1997-609 | 19951113 | <-- |
| | PL 181893 | B1 | 20011031 | PL 1995-320169 | 19951113 | <-- |
| | ZA 9509675 | A | 19960529 | ZA 1995-9675 | 19951114 | <-- |
| | IL 115970 | A1 | 19990620 | IL 1995-115970 | 19951114 | <-- |
| | FI 9701953 | A | 19970512 | FI 1997-1953 | 19970507 | <-- |
| | NO 9702198 | A | 19970513 | NO 1997-2198 | 19970513 | <-- |
| | US 5952342 | A | 19990914 | US 1998-40792 | 19980318 | <-- |
| PRAI | US 1994-339051 | B2 | 19941114 | <-- | | |
| | US 1995-539410 | A | 19951106 | <-- | | |
| | WO 1995-US14700 | W | 19951113 | <-- | | |

OS MARPAT 128:257439

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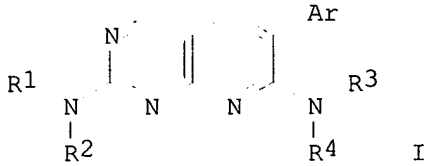


I

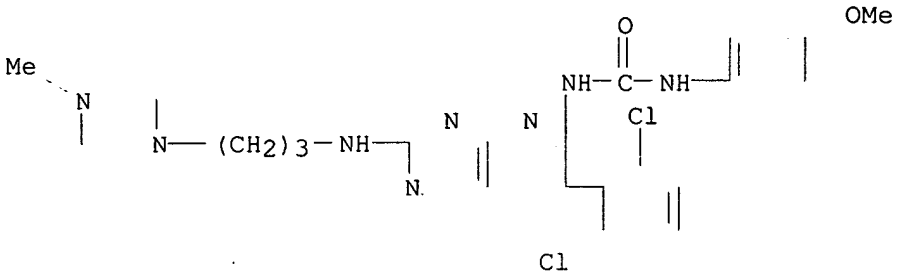
AB The title compds. [I; R1, R2, R4 = H, C1-8 alkyl, C2-8 alkenyl, etc.; R3 = C(O)R8, CO2R8, C(S)R8, etc.; R8 = H, C1-8 alkyl, C2-8 alkenyl, etc.; Ar = (un)substituted arom. ot heteroarom. selected from Ph, imidazolyl, pyrrolyl, etc.], inhibitors of protein tyrosine **kinase** which are esp. useful in treating atherosclerosis, restenosis, psoriasis, as well as bacterial infections, were prepd. and formulated. Thus, reaction of 2,7-diamino-6-(2,6-dichlorophenyl)pyrido[2,3-d]pyrimidine (prepn. described) with tert-Bu isocyanate in the presence of NaH in DMF afforded the urea I [R1 = R4 = H; R2 = R3 = C(O)NHtBu; Ar = 2,6-Cl2C6H3] which showed IC50 of 10.2 .mu.M against PDGF receptor tyrosine **kinase**.

IT **179342-64-4P 179342-65-5P 179342-66-6P**
**179342-67-7P 179342-68-8P 179342-69-9P**
**179342-71-3P 179342-73-5P 179342-74-6P**
**179342-76-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine **kinase** mediated cellular **proliferation**)

IT **179342-64-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine **kinase** mediated cellular **proliferation**)

RN 179342-64-4 HCAPLUS

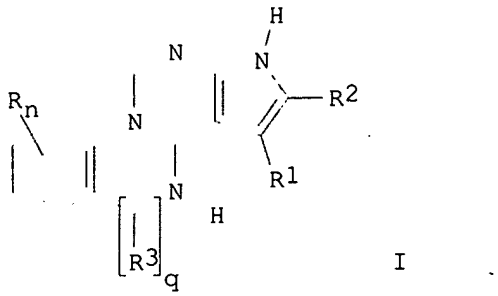
CN Urea, N-[6-(2,6-dichlorophenyl)-2-[[3-(4-methyl-1-piperazinyl)propyl]amino]pyrido[2,3-d]pyrimidin-7-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



L67 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:147332 HCAPLUS
DN 128:192664
TI Preparation of substituted pyrrolopyrimidines as **antitumor** agents
IN Traxler, Peter; Bold, Guido; Lang, Marc; Frei, Jorg
PA Novartis A.-G., Switz.; Traxler, Peter; Bold, Guido; Lang, Marc; Frei, Jorg
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9807726 | A1 | 19980226 | WO 1997-EP4564 | 19970821 <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CN 1194647 | A | 19980930 | CN 1996-196640 | 19960624 <-- |
| | AU 9742064 | A1 | 19980306 | AU 1997-42064 | 19970821 <-- |
| | AU 720429 | B2 | 20000601 | | |
| | EP 938486 | A1 | 19990901 | EP 1997-940108 | 19970821 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 2000516626 | T2 | 20001212 | JP 1998-510425 | 19970821 <-- |
| | US 6180636 | B1 | 20010130 | US 1999-242592 | 19990219 <-- |
| PRAI | CH 1996-2071 | A | 19960823 <-- | | |
| | WO 1997-EP4564 | A | 19970821 <-- | | |

OS MARPAT 128:192664
GI



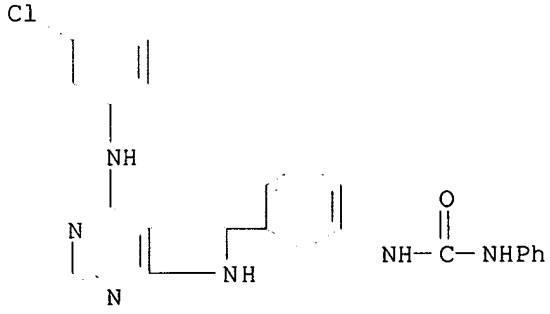
I

AB The title compds. [I; n = 0-3; q = 0-1; R = halo, lower alkyl, HOCH2, etc.; one of the radicals R1 and R2 = H, lower alkyl, and the other of the radicals R1 and R2 = (un)substituted Ph, amino-lower alkyl, piperidine-1-carbonyl, etc.], inhibitors of the tyrosine **kinase** activity of the receptor for the epidermal growth factor (EGF) and c-**erbB2kinase** and therefore useful as **antitumor** agents, were prepd. and formulated. Thus, hydrogenation of 4-(3-chloroanilino)-6-formyl-7H-pyrrolo[2,3-d]pyrimidine (prepn. described) with N-methylpiperazine in the presence of Raney Ni in DMPU, AcOH and MeOH afforded I [R = 3-Cl; R1 = H; R2 = 4-methylpiperazin-1-ylmethyl; q = 0]. Compds. I inhibit EGF-R-PTK activity by 50% (IC50), for example in a concn. of 0.0005-1 .mu.M, esp. from 0.001-1 .mu.M. Compds. I are effective at 0.5-2 g/day when administered to a patient of a body wt. of about 70 kg.

IT **203724-16-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted pyrrolopyrimidines as **antitumor** agents)

IT **203724-16-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted pyrrolopyrimidines as **antitumor** agents)

RN 203724-16-7 HCAPLUS
CN Urea, N-[3-[4-[(3-chlorophenyl)amino]-1H-pyrrolo[2,3-d]pyrimidin-6-yl]phenyl]-N'-phenyl- (9CI) (CA INDEX NAME)



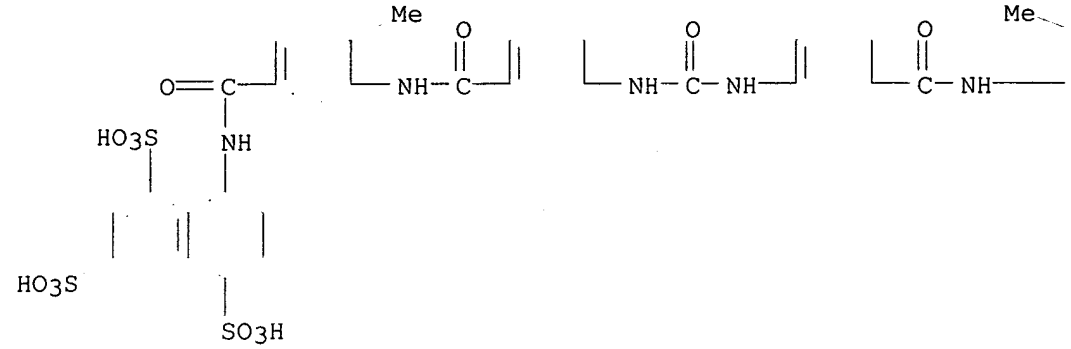
L67 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:803799 HCAPLUS
DN 128:66489
TI Compositions and methods for treating or preventing diseases of body

passageways
IN Hunter, William L.; Machan, Lindsay S.
PA Angiotech Pharmaceuticals, Inc., Can.; University of British Columbia; Hunter, William L.; Machan, Lindsay S.
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

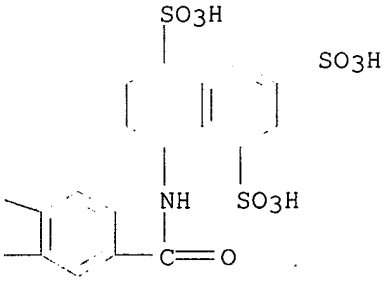
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9745105 | A1 | 19971204 | WO 1997-CA345 | 19970526 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9727604 | A1 | 19980105 | AU 1997-27604 | 19970526 <-- |
| AU 737078 | B2 | 20010809 | | |
| EP 914102 | A1 | 19990512 | EP 1997-921563 | 19970526 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1219872 | A | 19990616 | CN 1997-194908 | 19970526 <-- |
| BR 9710682 | A | 19990817 | BR 1997-10682 | 19970526 <-- |
| JP 2000511161 | T2 | 20000829 | JP 1997-541313 | 19970526 <-- |
| NO 9805463 | A | 19990121 | NO 1998-5463 | 19981123 <-- |
| KR 2000015944 | A | 20000315 | KR 1998-709500 | 19981124 <-- |
| PRAI US 1996-653207 | A | 19960524 <-- | | |
| WO 1997-CA345 | W | 19970526 <-- | | |

AB The present invention provides methods for treating or preventing diseases assocd. with body passageways, comprising the step of delivering to an external portion of the body passageway a therapeutic agent. Representative examples of therapeutic agents include anti-angiogenic factors, anti-**proliferative** agents, anti-inflammatory agents, and antibiotics. Pastes and nanosprays contg. polycaprolactone were prepd.
IT **145-63-1**, Suramin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. for treating or preventing diseases of body passageways)
IT **145-63-1**, Suramin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. for treating or preventing diseases of body passageways)
RN 145-63-1 HCAPLUS
CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L67 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:740435 HCAPLUS
DN 128:39550
TI Combinations of angiostatic compounds
IN Doshi, Rupa; Clark, Abbot F.
PA Clark, Abbot F., USA; Doshi, Rupa; Alcon Laboratories, Inc.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9741844 | A1 | 19971113 | WO 1997-US5574 | 19970403 <-- |
| | W: AU, CA, JP, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | AU 9724382 | A1 | 19971126 | AU 1997-24382 | 19970403 <-- |
| PRAI | US 1996-17096P | P | 19960509 <-- | | |
| | WO 1997-US5574 | W | 19970403 <-- | | |

OS MARPAT 128:39550
AB The present invention is directed to compns. contg. combinations of

angiostatic compds. (chromans or benzofurans and e.g., steroids ) and methods for their use in preventing pathol. neovascularization. Thus, 2-(5-hydroxy-2,4,6,7-tetramethyl-3,4-dihydrobenzo[1,2-b]furan-2-yl)ethyl 2-(6-methoxy-2-naphthyl)propionate (I) was prepd. by the reaction of 2-(5-hydroxy-2,4,6,7-tetramethyl-3,4-dihydrobenzo[1,2-b]furan-2-yl)ethanol with 6-methoxy-.alpha.-methylnaphthaleneacetic acid in the presence of dimethylaminopyridine and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide-HCl in THF. Thus, a topical ocular soln. contained I 1.0, another angiostatic compd.0.005-5.0%, benzalkonium chloride 0.01, HPMC 0.5, NaCl 0.8, Na phosphate 0.28, and disodium edetate 0.01%, NaOH/HCl qs pH 7.2, and water qs to 100 mL.

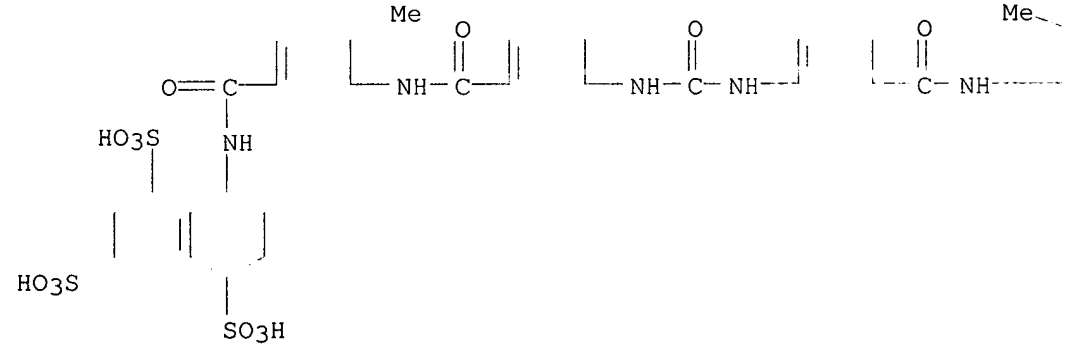
IT **145-63-1D**, Suramin, analogs
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg. combinations of angiostatic compds.)

IT **145-63-1D**, Suramin, analogs
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg. combinations of angiostatic compds.)

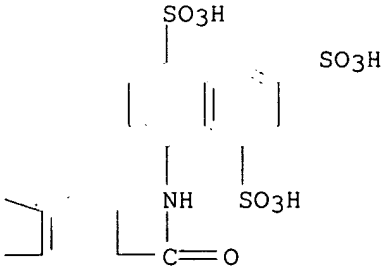
RN 145-63-1 HCAPLUS

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



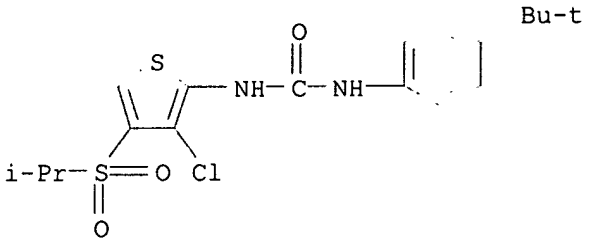

PAGE 1-B



L67 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:140236 HCAPLUS
DN 126:139899
TI Urea- and thiourea-type compounds capable of modulating tyrosine signal transduction
IN Tang, Peng Cho; McMahon, Gerald
PA Sugen, Inc., USA
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9640673 | A1 | 19961219 | WO 1996-US9077 | 19960604 <-- |
| | W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
| | RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| | US 5773459 | A | 19980630 | US 1995-486816 | 19950607 <-- |
| | AU 9660493 | A1 | 19961230 | AU 1996-60493 | 19960604 <-- |
| | JP 10175863 | A2 | 19980630 | JP 1996-359496 | 19961213 <-- |
| PRAI | US 1995-486816 | | 19950607 <-- | | |
| | WO 1996-US9077 | | 19960604 <-- | | |

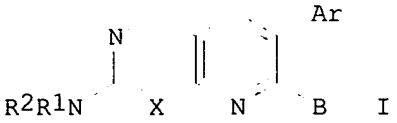
OS MARPAT 126:139899
AB The present invention relates to mols. capable of modulating tyrosine signal transduction to prevent and treat cell **proliferative** disorders or cell differentiation disorders assocd. with particular tyrosine **kinases** by inhibiting one or more abnormal tyrosine **kinase** activities. Four such compds. are N-[chloro-4-(isopropylsulfonyl)thien-2-yl]-N'-(4-t-butylphenyl)urea, N-[3-chloro-4-(isopropylsulfonyl)thien-2-yl]-N'-(3,5-ditrifluoromethylphenyl)urea, N-[2-(2,4-dichlorophenoxy)pyrid-5-yl]-N'-[4-trifluoromethyl(mercapto)phenyl]urea, and N-(4-cyanophenyl)-N'-[4-[(piperid-1-yl)sulfonyl]phenyl]thiourea. Disorders of Her2, EGFR, IGFR, PDGFR, met, Src and KDR/Flk-1 can be treated.
IT **186645-70-5P 186645-71-6P 186645-72-7P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea- and thiourea-type compds. capable of modulating tyrosine signal transduction)
IT **186645-70-5P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea- and thiourea-type compds. capable of modulating tyrosine signal transduction)
RN 186645-70-5 HCAPLUS
CN Urea, N-[3-chloro-4-[(1-methylethyl)sulfonyl]-2-thienyl]-N'-[4-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)




L67 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:467130 HCAPLUS
DN 125:114688
TI Preparation of 6-aryl pyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine **kinase**-mediated cellular **proliferation**
IN Blankley, Clifton John; Doherty, Annette Marian; Hamby, James Marino; Panek, Robert Lee; Schroeder, Mel Conrad; Showalter, Howard Daniel Hollis; Connolly, Cleo
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9615128 | A2 | 19960523 | WO 1995-US14700 | 19951113 <-- |
| | W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | US 5733913 | A | 19980331 | US 1995-539410 | 19951106 <-- |
| | AU 9641078 | A1 | 19960606 | AU 1996-41078 | 19951113 <-- |
| | AU 711426 | B2 | 19991014 | | |
| | EP 790997 | A2 | 19970827 | EP 1995-939129 | 19951113 <-- |
| | EP 790997 | B1 | 20000322 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | JP 10509452 | T2 | 19980914 | JP 1995-516240 | 19951113 <-- |
| | AT 190978 | E | 20000415 | AT 1995-939129 | 19951113 <-- |
| | SK 281724 | B6 | 20010710 | SK 1997-609 | 19951113 <-- |
| | PL 181893 | B1 | 20011031 | PL 1995-320169 | 19951113 <-- |
| | FI 9701953 | A | 19970512 | FI 1997-1953 | 19970507 <-- |
| | NO 9702198 | A | 19970513 | NO 1997-2198 | 19970513 <-- |
| PRAI | US 1994-339051 | A | 19941114 <-- | | |
| | US 1995-539410 | A | 19951106 <-- | | |
| | WO 1995-US14700 | W | 19951113 <-- | | |

OS MARPAT 125:114688
GI



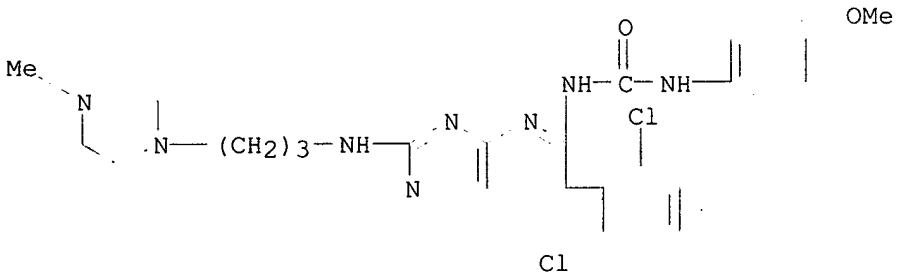

AB 6-Arylpyrido[2,3-d]pyrimidines and naphthyridines I [X = CH, N; B = halo, OH, NR3R4; R1, R2, R3, R4 = H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, Ar', amino, C1-8 alkylamino, di-C1-8 alkylamino, wherein the alkyl,

alkenyl, and alkynyl groups may be substituted by amino, OH, or 5- or 6-membered carbocyclic or heterocyclic ring; Ar, Ar' = (un)substituted arom. or heteroarom. groups; R1R2N or R3R4N can complete a ring having 3-6 C atoms and optionally contg. 1 or 2 heteroatoms; when X = N and B = NR3R4, one of R3 and R4 .noteq. H] or their pharmaceutically acceptable acid and base addn. salts, useful as inhibitors of protein tyrosine **kinase** and thus useful in treating cellular **proliferation** mediated thereby, are claimed. The compds. are esp. useful in treating atherosclerosis, restenosis, psoriasis, as well as bacterial infections. In an example, the IC50 of I [X = N, B = NHCONH2, R1 = H, R2 = Et2N(CH2)4 Ar = 2,6-Cl2C6H3; prepn. given] for inhibition of protein tyrosine **kinases** was 0.231 .mu.M for PDGF and 0.0954 for FGF.

IT **179342-64-4P 179342-65-5P 179342-66-6P**
**179342-67-7P 179342-68-8P 179342-69-9P**
**179342-71-3P 179342-73-5P 179342-74-6P**
**179342-76-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl pyridopyrimidines and naphthyridines for inhibiting protein tyrosine **kinase**-mediated cellular **proliferation**)

IT **179342-64-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl pyridopyrimidines and naphthyridines for inhibiting protein tyrosine **kinase**-mediated cellular **proliferation**)

RN 179342-64-4 HCAPLUS
CN Urea, N-[6-(2,6-dichlorophenyl)-2-[[3-(4-methyl-1-piperazinyl)propyl]amino]pyrido[2,3-d]pyrimidin-7-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)




L67 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:777654 HCAPLUS
DN 123:198839
TI Preparation of indolocarbazole derivatives to treat prostatic **cancer** and hypertrophy
IN Dionne, Craig A.; Contreras, Patricia C.; Murakata, Chikara
PA Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9427982 | A1 | 19941208 | WO 1994-US6082 | 19940527 <-- |

W: AU, CA, FI, HU, JP, KR, LK, NO, NZ, PL, RO, RU, UA
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

| | | | | | |
|---|---|---|---|---|---|
| CA 2163904 | AA | 19941208 | CA 1994-2163904 | 19940527 | <-- |
| AU 9469607 | A1 | 19941220 | AU 1994-69607 | 19940527 | <-- |
| AU 679752 | B2 | 19970710 | | | |
| EP 699204 | A1 | 19960306 | EP 1994-918168 | 19940527 | <-- |
| EP 699204 | B1 | 19980415 | | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE

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|---|---|---|---|---|---|
| EP 839814 | A2 | 19980506 | EP 1998-200023 | 19940527 | <-- |
| EP 839814 | A3 | 19980916 | | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE

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|---|---|---|---|---|---|
| AT 165097 | E | 19980515 | AT 1994-918168 | 19940527 | <-- |
| ES 2118414 | T3 | 19980916 | ES 1994-918168 | 19940527 | <-- |
| JP 2002504064 | T2 | 20020205 | JP 1995-501026 | 19940527 | <-- |
| FI 9505709 | A | 19960103 | FI 1995-5709 | 19951127 | <-- |
| NO 9504816 | A | 19960126 | NO 1995-4816 | 19951127 | <-- |

| | | | | |
|---|---|---|---|---|
| PRAI US 1993-69178 | A | 19930528 | <-- | |
| US 1993-96622 | A | 19930722 | <-- | |
| EP 1994-918168 | A3 | 19940527 | <-- | |
| WO 1994-US6082 | W | 19940527 | <-- | |

OS MARPAT 123:198839
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

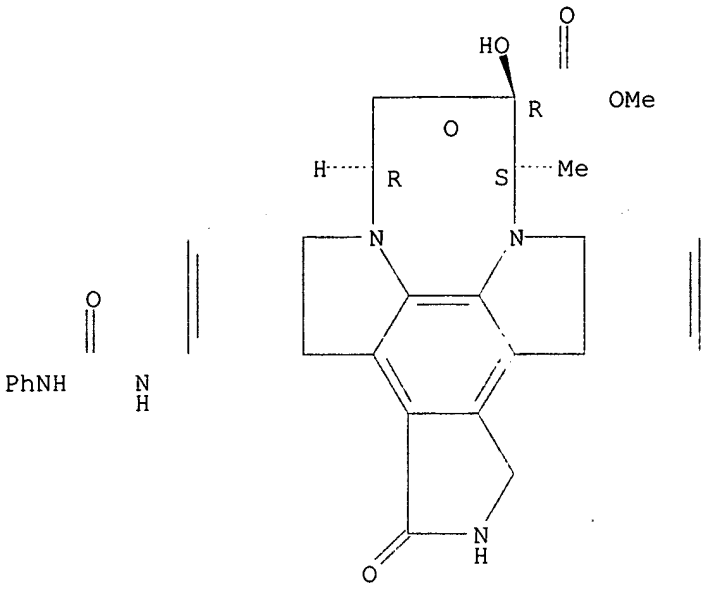
AB The title compds. [I; R = OH, alkoxy, acyloxy; R1, R2, R5, R6 = H, Cl, F, Br, I, NO2, CN, substituted ureido, etc.; X = H, CONHPh, etc.; Z1, Z2 = H, O (when combined)] [II; R1, R2, R5, R6 = H, halogen, NO2, CN, OH, substituted ureido; R3, R4 = H. alkyl, hydroxyalkyl, alkenyl; Z1, Z2 = H, O (when combined)], useful as inhibitors of tyrosine **kinase** activity assocd. with neurotropin receptors for treating benign prostatic hypertrophy or prostate **cancer**, are prepd. Thus, oxadiazepine I (R = OH, R1 = R2 = R5 = R6 = Z1 = Z2 = H, X = CONHCH2CH2OH) was prepd. and demonstrated a IC50 of 0.038 .mu.M against the Tsu-Pr1 human prostate **cancer** cell line.

IT **121664-76-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed compd.; prepn. of indolocarbazole derivs. to treat prostatic **cancer** and benign prostatic hypertrophy)

IT **121664-76-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed compd.; prepn. of indolocarbazole derivs. to treat prostatic **cancer** and benign prostatic hypertrophy)

RN 121664-76-4 HCAPLUS
CN 9,12-Epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-9-methyl-1-oxo-16-[[(phenylamino)carbonyl]amino]-, methyl ester, (9S,10R,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L67 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:400902 HCAPLUS
DN 121:902
TI Therapeutic-binding protein conjugate for inhibitor of vascular smooth muscle cells
IN Kunz, Lawrence Leroy
PA Neorx Corp., USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 12

| | PATENT NO. | KIND | DATE | | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|---|
| PI | WO 9407529 | A1 | 19940414 | | WO 1992-US8220 | 19920925 | <-- |
| | W: CA, JP, US | | | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE | | | | | | |
| | EP 752885 | A1 | 19970115 | | EP 1994-911762 | 19920925 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE | | | | | | |
| | US 6251920 | B1 | 20010626 | | US 1998-82643 | 19980521 | <-- |
| | US 6262079 | B1 | 20010717 | | US 1999-306606 | 19990506 | <-- |
| | US 6268390 | B1 | 20010731 | | US 1999-470662 | 19991222 | <-- |
| | US 2002013275 | A1 | 20020131 | | US 2001-910388 | 20010720 | <-- |
| | US 2002040064 | A1 | 20020404 | | US 2001-910387 | 20010720 | <-- |
| PRAI | US 1991-767254 | A2 | 19910927 | <-- | | | |
| | WO 1992-US8220 | W | 19920925 | <-- | | | |
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| | US 1994-242161 | A2 | 19940512 | <-- | | | |
| | US 1995-389712 | A1 | 19950215 | <-- | | | |
| | US 1995-450793 | A1 | 19950525 | <-- | | | |
| | US 1995-486334 | A3 | 19950607 | <-- | | | |
| | US 1998-82643 | A1 | 19980521 | | | | |
| | US 1998-113733 | A1 | 19980710 | | | | |
| | US 1999-470662 | A1 | 19991222 | | | | |

AB Methods are provided for inhibiting stenosis following vascular trauma or

disease in a mammalian host, comprising administering to the host a therapeutically effective dosage of a therapeutic conjugate contg. a vascular smooth muscle binding protein that assocs. in a specific manner with a cell surface of the vascular smooth muscle cell, coupled to a therapeutic agent that inhibits a cellular activity of the muscle cell. Prepn. and testing of Roridin A-monoclonal antibody conjugates is described.

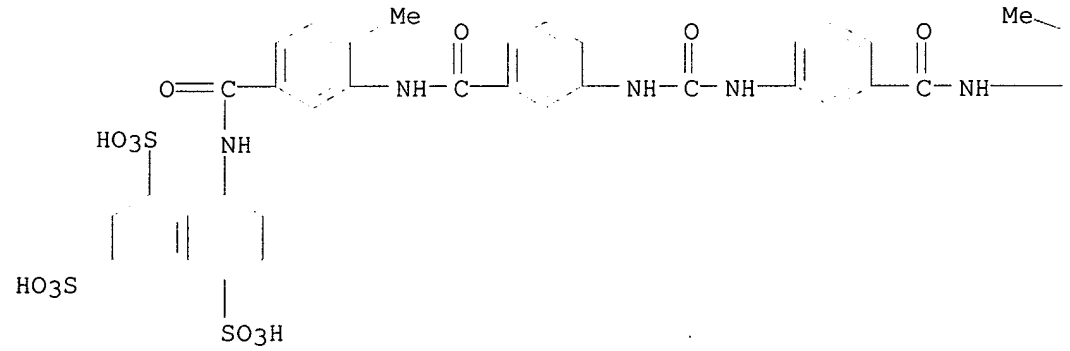
IT **145-63-1D**, Suramin, conjugates with vascular smooth muscle cell-specific binding proteins
RL: BIOL (Biological study)
(for noncytocidal vascular smooth muscle cell inhibition)

IT **145-63-1D**, Suramin, conjugates with vascular smooth muscle cell-specific binding proteins
RL: BIOL (Biological study)
(for noncytocidal vascular smooth muscle cell inhibition)

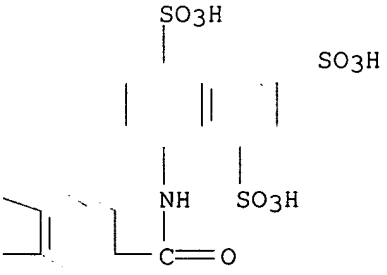
RN 145-63-1 HCAPLUS

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 1-B




L67 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:217715 HCAPLUS

DN 120:217715
TI Quinazoline tyrosine **kinase**-inhibiting **anticancer** agents
IN Barker, Andrew J.
PA Zeneca Ltd., UK
SO Can. Pat. Appl., 99 pp.
CODEN: CPXXEB
DT **Patent**
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | CA 2086968 | AA | 19930721 | CA 1993-2086968 | 19930108 | <-- |
| | CA 2086968 | C | 19980623 | | | |
| | ZA 9300015 | A | 19930720 | ZA 1993-15 | 19930104 | <-- |
| | AU 9331010 | A1 | 19930722 | AU 1993-31010 | 19930104 | <-- |
| | AU 661533 | B2 | 19950727 | | | |
| | HU 63153 | A2 | 19930728 | HU 1993-94 | 19930115 | <-- |
| | EP 566226 | A1 | 19931020 | EP 1993-300270 | 19930115 | <-- |
| | EP 566226 | B1 | 19951108 | | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| | AT 130000 | E | 19951115 | AT 1993-300270 | 19930115 | <-- |
| | ES 2078798 | T3 | 19951216 | ES 1993-300270 | 19930115 | <-- |
| | CZ 282038 | B6 | 19970416 | CZ 1993-43 | 19930118 | <-- |
| | NO 9300178 | A | 19930721 | NO 1993-178 | 19930119 | <-- |
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| | SK 281551 | B6 | 20010510 | SK 1993-16 | 19930119 | <-- |
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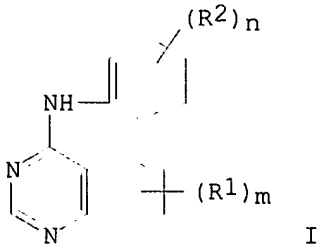
| | JP 06073025 | A2 | 19940315 | JP 1993-26577 | 19930216 | <-- |
| | JP 2994165 | B2 | 19991227 | | | |
| | US 5457105 | A | 19951010 | US 1994-284293 | 19940802 | <-- |
| | US 5616582 | A | 19970401 | US 1995-490666 | 19950615 | <-- |
| PRAI | GB 1992-1095 | A | 19920120 | <-- | | |
| | GB 1992-13572 | A | 19920626 | <-- | | |
| | GB 1992-23735 | A | 19921112 | <-- | | |
| | US 1993-5280 | B1 | 19930119 | <-- | | |
| | US 1994-284293 | A1 | 19940802 | <-- | | |

OS MARPAT 120:217715
GI




I

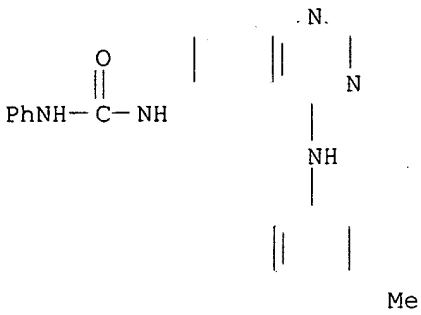
AB The title compds. I [R1 = HO, (un)substituted amino, carboxy, carbamoyl, ureido, etc.; R2 = H, HO, halogen, CF3, NH2, NO2, CN, (un)substituted C1-4 alkyl, etc.; m = 1-3; n = 1, 2], useful as tyrosine **kinase** -inhibiting **anticancer** agents (no data), are prepd. and I-contg. formulations presented. Thus, 4-chloro-6,7-dimethoxyquinazoline was condensed with 3-MeC6H4NH2, producing 6,7-dimethoxy-4-(3'-methylanilino)quinazoline hydrochloride, m.p. 248-249.degree..
IT **153437-28-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as tyrosine **kinase**-inhibiting **anticancer** agent)

IT **153437-28-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as tyrosine **kinase**-inhibiting **anticancer** agent)

RN 153437-28-6 HCAPLUS

CN Urea, N-[4-[(3-methylphenyl)amino]-6-quinazolinyl]-N'-phenyl- (9CI) (CA INDEX NAME)




L67 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1993:167454 HCAPLUS

DN 118:167454

TI Antibodies against the **urokinase** plasminogen activator receptor (u-PAR) and their use

IN Danoe, Keld; Roenne, Ebbe; Behrendt, Niels; Ellis, Vincent; Hoeyer-Hansen, Gunilla; Pyke, Charles; Bruenner, Nils

PA Cancerforskningsfondet af 1989, Den.

SO PCT Int. Appl., 215 pp.
CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | WO 9207083 | A1 | 19920430 | WO 1991-DK319 | 19911018 | <-- |
| | W: AU, CA, FI, HU, JP, KR, NO, SU, US | | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | | |
| | AU 9187572 | A1 | 19920520 | AU 1991-87572 | 19911018 | <-- |
| | AU 661978 | B2 | 19950817 | | | |
| | EP 574391 | A1 | 19931222 | EP 1991-918632 | 19911018 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | | |
| | JP 07500486 | T2 | 19950119 | JP 1991-517643 | 19911018 | <-- |
| | WO 9308301 | A1 | 19930429 | WO 1992-DK306 | 19921019 | <-- |
| | W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US | | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | | |
| | AU 9229412 | A1 | 19930521 | AU 1992-29412 | 19921019 | <-- |
| | EP 637967 | A1 | 19950215 | EP 1992-923698 | 19921019 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE | | | | | |
| | US 6113897 | A | 20000905 | US 1995-580166 | 19951228 | <-- |
| PRAI | WO 1990-DK270 | A | 19901018 | <-- | | |
| | DK 1992-564 | | 19920430 | <-- | | |
| | US 1989-334613 | A2 | 19890407 | <-- | | |
| | US 1989-374854 | B2 | 19890703 | <-- | | |
| | WO 1990-DK90 | A1 | 19900409 | <-- | | |

| | | | |
|---|---|---|---|
| WO 1991-DK319 | A | 19911018 | <-- |
| US 1991-824189 | B2 | 19911206 | <-- |
| WO 1992-DK306 | A | 19921019 | <-- |
| US 1993-85122 | A3 | 19930617 | <-- |

AB Monoclonal and polyclonal antibodies are provided which are directed against u-PAR or a subsequence, analog, or glycosylation variant thereof. Antibodies are disclosed which react with free u-PAR or with complexes between u-PA and u-PAR which can (1) catch u-PAR in an ELISA; (2) detect u-PAR, e.g. in blotting; (3) in radioimmunopptn. assay ppt. purified u-PAR in intact or fragment form; (4) detect u-PAR immunohistochem., e.g. in immunostaining of **cancer** cells, such as in tissue sections or at the invasive front; and (5) inhibit the binding of pro-u-PA and active u-PA and thereby inhibit cell-surface plasminogen activation. Methods are disclosed (1) for detecting or quantifying u-PAR; (2) for targeting a diagnostic to a cell contg. a u-PAR on the surface; and (3) for preventing or counteracting proteolytic activity in a mammal. Methods for selecting a substance suitable for inhibiting the u-PA/u-PAR interaction, for preventing or counteracting localized proteolytic activity in a mammal, or for inhibiting invasion and/or **metastasis** comprise the use of the antibodies and of nude mice inoculated with human **cancer** cells which are known to invade and/or **metastasize** in mice and having a distinct color (produced by an enzyme and chromogenic substrate) which is different from that of the cells of the mouse. Prepn. of the antibodies is described, as are isolation and characterization of u-PAR from U937 cells and immunochem. procedures using the antibodies. Monoclonal antibodies against u-PA inhibited the invasive and **metastatic** process in mice.

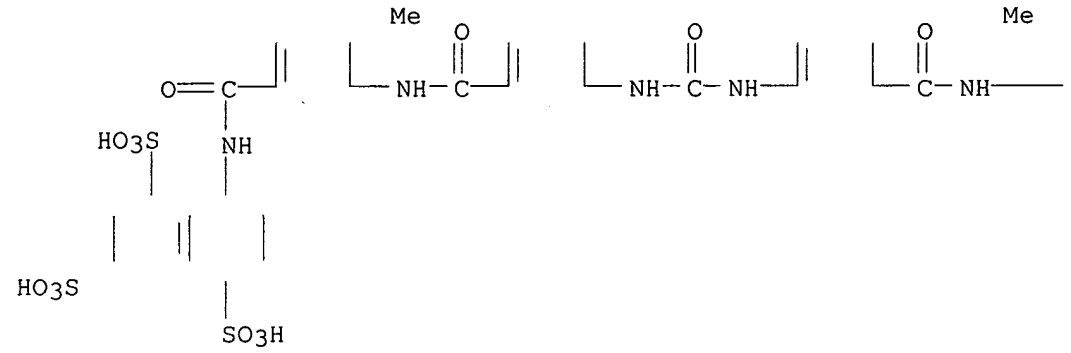
IT **145-63-1**, Suramin
RL: PRP (Properties)
(**urokinase**-type plasminogen activator interaction with receptor in presence of, immunochem. screening assay for, antibodies for)

IT **145-63-1**, Suramin
RL: PRP (Properties)
(**urokinase**-type plasminogen activator interaction with receptor in presence of, immunochem. screening assay for, antibodies for)

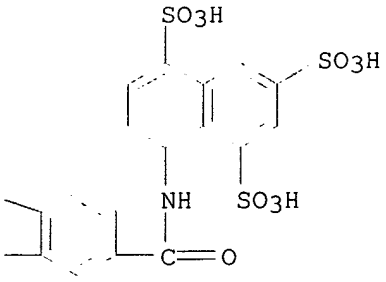
RN 145-63-1 HCAPLUS

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



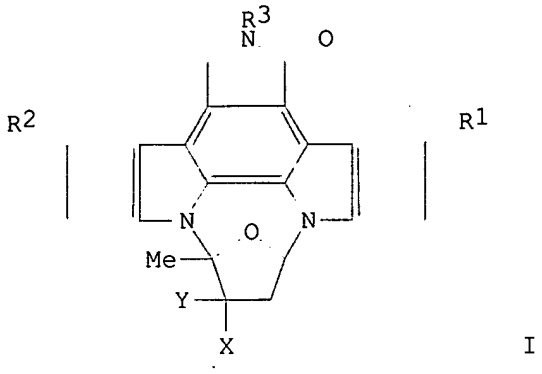
PAGE 1-B



L67 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1989:477750 HCAPLUS
DN 111:77750
TI K-252 derivatives as protein **kinase** C inhibitors, their preparation, and formulations containing them
IN Hirata, Tadashi; Mochida, Kenichi; Muragata, Tsutomu; Takahashi, Mitsuru; Kase, Hiroshi; Yamada, Koji; Iwahashi, Kazuyuki; Sato, Akira; Kasai, Masaji; et al.
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 40 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 63295588 | A2 | 19881201 | JP 1987-327858 | 19871224 <-- |
| | JP 08026036 | B4 | 19960313 | | |
| PRAI | JP 1987-12719 | | 19870122 <-- | | |

OS MARPAT 111:77750
GI



I

AB The title compds. I [R1,R2 = H, Me, hydroxymethyl, lower alkoxymethyl, alkylthiomethyl, etc.; R3 = H, Cl, lower alkanoyl, carbamoyl, etc.; X = hydroxymethyl, CO2H, lower alkoxycarbonyl, etc.; Y = OH, lower alkanoyloxy, etc., or YX = OCMe2OCH2, OCSNHCH2, etc.; provisos are given (for example, when X = hydroxymethyl, CO2H, lower alkoxycarbonyl, at least one of R1-R3 must be other than H)], useful as protein **kinase** C inhibitors, were prepd. Treatment of I (R1 = NH2, R2 = H, R3 = Ac, X = CO2Me, Y = OAc) (prepn. given) with MeONa, followed by workup and acidification, gave I.HCl (R1 = NH2, R2 = R3 = H, X = CO2Me, Y = OH) (II). II in vitro exhibited an IC50 of 0.175 .mu.g/mL against protein **kinase** C. A tablet formulation contg. I (R1 = R2 = R3 = H, X = CH:NOH, Y = OH) 100, starch 18, lactose 40, Ca CM-cellulose 10 g, hydroxypropylcellulose, and Mg stearate (amt. unspecified) is given.

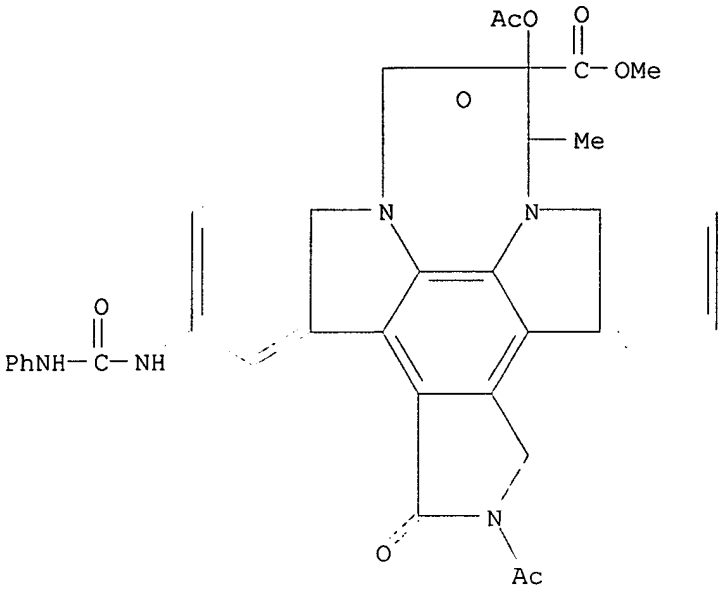
IT **121665-13-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of protein **kinase** C inhibitor)

IT **121664-76-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as protein **kinase** C inhibitor)

IT **121665-13-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of protein **kinase** C inhibitor)

RN 121665-13-2 HCAPLUS

CN 9,12-Epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2-acetyl-10-(acetyloxy)-2,3,9,10,11,12-hexahydro-9-methyl-1-oxo-16-[[(phenylamino)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)




=> d l74 bib abs hitrn fhitstr tot

L74 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:241346 HCAPLUS
DN 136:279203
TI Substituted phenyl derivatives, their preparation and use
IN Dahl, Bjarne H.; Christophersen, Palle
PA Den.
SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 837,166.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | US 2002037905 | A1 | 20020328 | US 2001-923458 | 20010808 | <-- |
| | WO 9847879 | A1 | 19981029 | WO 1998-DK162 | 19980421 | <-- |
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| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | | |
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| | EP 977741 | A1 | 20000209 | EP 1998-914851 | 19980421 | <-- |
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| | BR 9808938 | A | 20000801 | BR 1998-8938 | 19980421 | <-- |
| | JP 2001521532 | T2 | 20011106 | JP 1998-544759 | 19980421 | <-- |
| | US 6297261 | B1 | 20011002 | US 1999-402165 | 19990930 | <-- |
| | WO 2000024707 | A1 | 20000504 | WO 1999-DK575 | 19991019 | |
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MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| | US 2002032210 | A1 | 20020314 | US 2001-837166 | 20010419 |
| PRAI | DK 1997-452 | A | 19970422 | <-- | |
| | WO 1998-DK162 | W | 19980421 | | |
| | DK 1998-1362 | A | 19981022 | | |
| | US 1999-402165 | A2 | 19990930 | | |
| | WO 1999-DK575 | A1 | 19991019 | | |
| | US 2001-837166 | A2 | 20010419 | | |

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; 1 of R1-R3 = acidic functional group having pKa < 8 or a group convertible in vivo to such a group; R4, R5 and the others of R1-R3 = independently H, alkyl, alkoxy, OH, halo, CF3, cyano, NO2, amino, etc.; Y = C(X)NR0, NR0C(X)NR00, etc.; R0, R00 = independently H, alkyl; X = O, S; R11-R15 = independently H, alkyl, alkoxy, OH, halo, CF3, cyano (substituted) aryl, heteroaryl, phenylamino, etc.] were prepd. Thus, 3-Trifluoromethylphenyl isocyanate and 2-aminobenzoic acid were stirred in PhMe to give N-3-trifluoromethylphenyl, N'-2-carboxyphenyl urea (II). The compds. are useful as chloride channel blockers. N-3-trifluoromethylphenyl-N'-[4'-(dimethylsulfamoyl)-2-(1H-tetrazol-5-yl)-4-biphenyl]urea (III) blocked erythrocyte chloride channels with KD = 0.3 .mu.M.

IT **265646-59-1P 405520-02-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **1566-81-0P 2164-95-6P 200193-42-6P**
**265646-51-3P 265646-52-4P 265646-53-5P**
**265646-54-6P 265646-55-7P 265646-57-9P**
**265646-60-4P 265646-61-5P 265646-62-6P**
**265646-63-7P 265646-64-8P 265646-65-9P**
**265646-66-0P 265646-67-1P 265646-68-2P**
**265646-69-3P 265646-71-7P 265646-72-8P**
**265646-75-1P 265646-76-2P 265646-77-3P**
**265646-78-4P 265646-79-5P 265646-80-8P**
**265646-81-9P 265646-82-0P 265646-83-1P**
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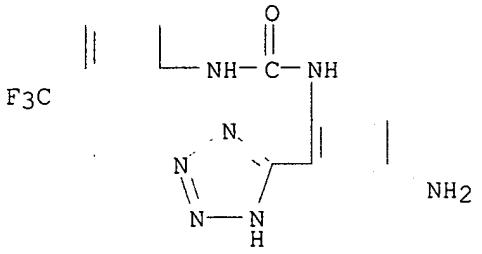
**405520-69-6P 405520-74-3P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **405520-70-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **265646-59-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

RN 265646-59-1 HCAPLUS
CN Urea, N-[4-amino-2-(1H-tetrazol-5-yl)phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



L74 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:521916 HCAPLUS
DN 135:107152
TI Preparation of N,N'-diphenyl ureas as IL-8 receptor antagonists
IN Widdowson, Katherine Louisa; Veber, Daniel Frank; Jurewicz, Anthony Joseph; Hertzberg, Robert Philip; Rutledge, Melvin Clarence, Jr.
PA Smithkline Beecham Corp., USA
SO U.S., 51 pp., Cont.-in-part of U.S. 58,86,044.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 6262113 | B1 | 20010717 | US 1998-125279 | 19980814 <-- |
| US 5886044 | A | 19990323 | US 1996-641990 | 19960320 <-- |
| WO 9729743 | A1 | 19970821 | WO 1996-US13632 | 19960821 <-- |

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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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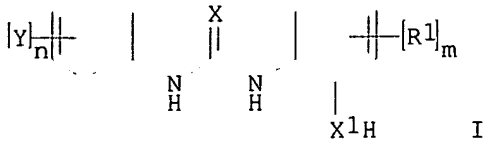
| PRAI US 1996-641990 | A2 | 19960320 | <-- |
| WO 1996-US13632 | W | 19960821 | <-- |
| US 1995-390260 | B2 | 19950217 | <-- |
| WO 1996-US2260 | A | 19960216 | <-- |

OS MARPAT 135:107152
GI



I

AB The title compds. [I; X = O; X1 = O, S; R1 = H, halo, NO2, etc.; two R1 moieties together may form O(CH2)sO, 5-6 membered unsatd. ring; s = 1-3; Y = H, halo, NO2, etc.; two Y moieties together may form O(CH2)sO, 5-6 membered unsatd. ring; n, m = 1-3], useful for treating a chemokine mediated disease, wherein the chemokine is one which binds to an IL-8 .alpha. or .beta. receptor, were prepd. Thus, reacting Me 4-amino-3-hydroxybenzoate with Ph isocyanate afforded 90% I [X = O; R = OH; R1 = 4-CO2Me; m = 1; Y = H]. All of the exemplified compds. I showed an IC50 from about 45 to about < 1 .mu.g/mL against IL-8 receptor binding. All of these compds. were also found to be inhibitors of Gro-.alpha. binding at about the same level.

IT **160383-79-9P 182497-99-0P 182498-47-1P**
**182498-79-9P 182498-99-3P 182499-02-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N,N'-diphenyl ureas as IL-8 receptor antagonists)

IT **85915-46-4P 88846-90-6P 92949-89-8P**
**117745-32-1P 160383-78-8P 160383-90-4P**
**182498-03-9P 182498-07-3P 182498-11-9P**
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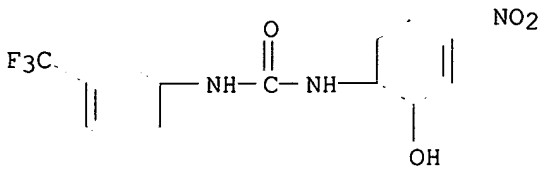
**210358-66-0P 210358-67-1P 210358-68-2P**
**210358-69-3P 210358-70-6P 210358-71-7P**
**210358-72-8P 210358-73-9P 210358-74-0P**
**210358-75-1P 210358-77-3P 210358-78-4P**
**210358-79-5P 210358-80-8P 210358-81-9P**
**210358-84-2P 210358-86-4P 210358-88-6P**
**210358-93-3P 210358-95-5P 210358-97-7P**
**210358-98-8P 210358-99-9P 210359-00-5P**
**210359-01-6P 210359-02-7P 210359-03-8P**
**210359-04-9P 210359-05-0P 210359-06-1P**
**210359-07-2P 210359-08-3P 222172-42-1P**
**313688-79-8P 313688-80-1P 350044-75-6P**
**350044-78-9P 350044-79-0P 350044-80-3P**
**350044-81-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N,N'-diphenyl ureas as IL-8 receptor antagonists)

IT **182499-76-9P 182499-79-2P 182499-88-3P**
**182500-24-9P 182500-25-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N,N'-diphenyl ureas as IL-8 receptor antagonists)

IT **160383-79-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N,N'-diphenyl ureas as IL-8 receptor antagonists)

RN 160383-79-9 HCAPLUS
CN Urea, N-(2-hydroxy-4-nitrophenyl)-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

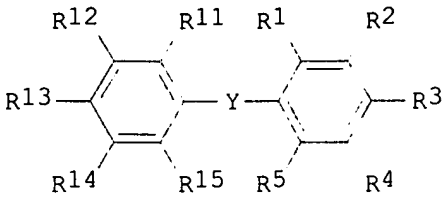



RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:290984 HCAPLUS
DN 132:308142
TI Preparation of diarylureas and related compounds as chloride channel blockers.
IN Dahl, Bjarne H.; Christophersen, Palle
PA Neurosearch A/s, Den.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | WO 2000024707 | A1 | 20000504 | WO 1999-DK575 | 19991019 | |
| | W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| | AU 9963259 | A1 | 20000515 | AU 1999-63259 | 19991019 | |
| | BR 9914638 | A | 20010703 | BR 1999-14638 | 19991019 | |
| | EP 1123274 | A1 | 20010816 | EP 1999-950505 | 19991019 | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | | |
| | US 2002032210 | A1 | 20020314 | US 2001-837166 | 20010419 | |
| | NO 2001001956 | A | 20010420 | NO 2001-1956 | 20010420 | |
| | US 2002037905 | A1 | 20020328 | US 2001-923458 | 20010808 | <-- |
| PRAI | DK 1998-1362 | A | 19981022 | | | |
| | DK 1997-452 | A | 19970422 | <-- | | |
| | WO 1998-DK162 | W | 19980421 | | | |
| | US 1999-402165 | A2 | 19990930 | | | |
| | WO 1999-DK575 | W | 19991019 | | | |
| | US 2001-837166 | A2 | 20010419 | | | |

OS MARPAT 132:308142
GI




I

AB Title compds. [I; 1 of R1-R3 = acidic functional group having pKa<8 or a group convertible in vivo to such a group; R4, R5 and the others of R1-R3 = H, alkyl, alkoxy, OH, halo, CF3, cyano, NO2, amino, etc.; Y = C(:X)NR0, NR0C(:X)NR00, etc.; R0, R00 = H, alkyl; X = O, S; R11-R15 = H, alkyl, alkoxy, OH, halo, CF3, cyano, (substituted) aryl, heteroaryl, phenylamino, etc.], were prepd. Thus, 3-trifluoromethylphenyl isocyanate and 2-aminobenzoic acid were stirred in PhMe to give N-3-trifluoromethylphenyl-N'-2-carboxyphenyl urea. N-3-trifluoromethylphenyl-N'-[4'-(dimethylsulfamoyl)-2-(1H-tetrazol-5-yl)-4-biphenyl]urea blocked erythrocyte chloride channels with KD = 0.3 .mu.M.

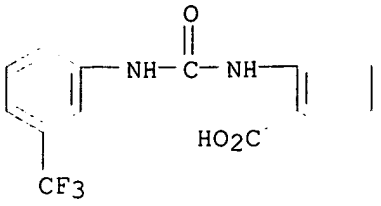
IT **1566-81-0P 2164-95-6P 200193-42-6P**
**265646-51-3P 265646-52-4P 265646-53-5P**
**265646-54-6P 265646-55-7P 265646-57-9P**
**265646-59-1P 265646-60-4P 265646-61-5P**
**265646-62-6P 265646-63-7P 265646-64-8P**
**265646-65-9P 265646-66-0P 265646-67-1P**
**265646-68-2P 265646-69-3P 265646-70-6P**
**265646-71-7P 265646-72-8P 265646-73-9P**
**265646-74-0P 265646-75-1P 265646-76-2P**
**265646-77-3P 265646-78-4P 265646-79-5P**
**265646-80-8P 265646-81-9P 265646-82-0P**
**265646-83-1P 265646-84-2P 265646-85-3P**
**265646-86-4P 265646-87-5P 265646-88-6P**
**265646-89-7P 265646-90-0P 265646-91-1P**
**265646-92-2P 265646-94-4P 265646-95-5P**
**265646-96-6P 265646-97-7P 265646-98-8P**
**265646-99-9P 265647-00-5P 265647-01-6P**
**265647-02-7P 265647-03-8P 265647-04-9P**
**265647-07-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **265647-06-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **1566-81-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

RN 1566-81-0 HCAPLUS

CN Benzoic acid, 2-[[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

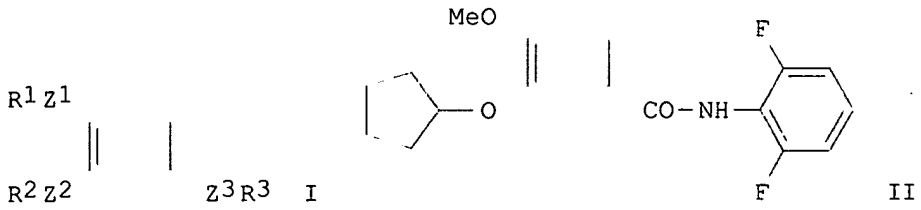


RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:505666 HCAPLUS
DN 131:144417
TI N-(Hetero)aryl-3,4-(cyclo)alkoxybenzamides and analogs useful as **tumor** necrosis factor and c-AMP phosphodiesterase inhibitors
IN Fenton, Garry; Morley, Andrew David; Palfreyman, Malcolm Norman; Ratcliffe, Andrew James; Harp, Brian William; Thurairatnam, Sukanthini; Vacher, Bernard Yvon Jack; Ashton, Michael John; Cook, David Charles; Hills, Susan Jacqueline; McFarlane, Ian Michael; Vicker, Nigel
PA Rhone-Poulenc Rorer Ltd., UK
SO U.S., 48 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | US 5935978 | A | 19990810 | US 1993-98178 | 19930728 | <-- |
| | ZA 9200547 | A | 19930503 | ZA 1992-547 | 19920127 | <-- |
| | WO 9212961 | A1 | 19920806 | WO 1992-GB153 | 19920128 | <-- |
| | W: AU, CA, CS, FI, HU, JP, KR, NO, PL, RU, US | | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | | |
| | AU 9211881 | A1 | 19920827 | AU 1992-11881 | 19920128 | <-- |
| | AU 664694 | B2 | 19951130 | | | |
| | EP 569414 | A1 | 19931118 | EP 1992-903462 | 19920128 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | | |
| | JP 06504782 | T2 | 19940602 | JP 1992-503280 | 19920128 | <-- |
| | PL 169994 | B1 | 19960930 | PL 1992-300142 | 19920128 | <-- |
| | CZ 281894 | B6 | 19970312 | CZ 1993-1528 | 19920128 | <-- |
| | NO 9302701 | A | 19930921 | NO 1993-2701 | 19930727 | <-- |
| | ZA 9305448 | A | 19940519 | ZA 1993-5448 | 19930728 | <-- |
| | FI 9500375 | A | 19950127 | FI 1995-375 | 19950127 | <-- |
| | US 5679696 | A | 19971021 | US 1995-484805 | 19950607 | <-- |
| | US 5698711 | A | 19971216 | US 1995-487377 | 19950607 | <-- |
| | US 5840724 | A | 19981124 | US 1997-881888 | 19970624 | <-- |
| | US 6255326 | B1 | 20010703 | US 1999-239075 | 19990127 | <-- |
| | US 6096768 | A | 20000801 | US 1999-301877 | 19990429 | <-- |
| PRAI | GB 1991-1777 | A | 19910128 | <-- | | |
| | GB 1991-17727 | A | 19910816 | <-- | | |
| | WO 1992-GB153 | B2 | 19920128 | <-- | | |
| | GB 1992-15989 | A | 19920728 | <-- | | |
| | GB 1992-16005 | A | 19920728 | <-- | | |
| | GB 1992-16006 | A | 19920728 | <-- | | |
| | GB 1992-16008 | A | 19920728 | <-- | | |
| | GB 1992-16764 | A | 19920807 | <-- | | |
| | GB 1993-10633 | A | 19930521 | <-- | | |
| | GB 1993-10938 | A | 19930527 | <-- | | |
| | GB 1993-11281 | A | 19930601 | <-- | | |
| | GB 1993-14847 | A | 19930716 | <-- | | |
| | US 1993-98178 | A3 | 19930728 | <-- | | |

US 1995-484805 A3 19950607 <--
OS MARPAT 131:144417
GI



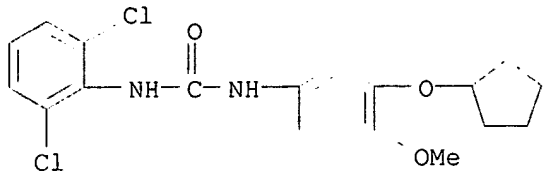

AB Title compds. (I) [R1 = lower alkyl; R2 = (un)substituted cycloalkyl, (un)substituted cycloalkenyl, (un)substituted or oxidized cyclothioalkyl, or (un)substituted or oxidized cyclothioalkenyl; R3 = (un)substituted (hetero)aryl; Z, Z1, Z2 = independently O or S; Z3 = C(:Z)NH] and their N-oxides and salts were prepd. for pharmaceutical use as **tumor** necrosis factor and cAMP phosphodiesterase inhibitors. Thus, 3-cyclopentyloxy-4-methoxybenzoyl chloride (prepn. given) in CH2Cl2 was added dropwise to 2,6-difluoroaniline in triethylamine and CH2Cl2 and refluxed for 4 h to yield N-(2,6-difluorophenyl)-3-cyclopentyloxy-4-methoxybenzamide (II). Compds. of the invention were tested for inhibitory effects on PDE activity and eosinophil superoxide generation, effects on tracheal smooth muscle contractility, in vivo bronchodilator actions and antigen(ovalbamin)-induced eosinophilia, in vitro inhibitory effects on TNF-.alpha. release by human monocytes, and inhibitory effects on antigen-induced bronchoconstriction in conscious guinea-pigs and serum TNF-.alpha. levels in LPS-challenged mice. Compds. showed 10,000-fold to 50-fold more selectivity for cAMP phosphodiesterase IV than cyclic nucleotide phosphodiesterase types I, III, or V and have IC50 values ranging from 0.1 nM to 40 .mu.M for PDE activity. At concns. from 5x10-9M to 10-5M, preferably 5x10-9 to 10-7, compds. produced about 50% relaxation of guinea-pig tracheal strips. When administered at EDs of 4 to 1000 .mu.g/kg, preferably 4 to 50 .mu.g/kg, compds. produced 30% to 90% decrease in bronchospasm without any significant effect on blood pressure. At oral doses of 1 to 50 mg/kg, preferably 1 to 10 mg/kg, and inhaled doses of 4 to 1000 .mu.g/kg, preferably 4 to 50 .mu.g/kg, compds. inhibited by at least 50% ovalbumin-induced eosinophilia in guinea-pigs. Compds. produced 50% inhibition of LPS-induced TNF-.alpha. release from human PBMs at concns. of 10-9M to 10-6M, preferably 10-9M to 10-8 M. At doses of 1 to 1000 .mu.g/kg (i.t.), preferably 1 to 20 .mu.g/kg (i.t.), compds. inhibited antigen-induced bronchoconstriction by up to 80%. Compds. inhibited LPS-induced serum TNF-.alpha. at doses of 10 to 10,000 .mu.g/kg, preferably 10 to 250 .mu.g/kg. Compds. showed very low mammalian toxicity levels. Twenty-one compns. of the title compds. for gelatin capsules or dry powder inhalers were also prepd.

IT **159782-48-6P**, N-(2,6-Dichlorophenyl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea **159782-49-7P**, N-(3,5-Dichloropyrid-4-yl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(hetero)aryl 3,4-(cyclo)alkoxybenzamides and analogs useful as **tumor** necrosis factor and c-AMP phosphodiesterase inhibitors)

IT **159782-48-6P**, N-(2,6-Dichlorophenyl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-(hetero)aryl 3,4-(cyclo)alkoxybenzamides and analogs useful as **tumor** necrosis factor and c-AMP phosphodiesterase inhibitors)

RN 159782-48-6 HCAPLUS
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(2,6-dichlorophenyl)-(9CI) (CA INDEX NAME)

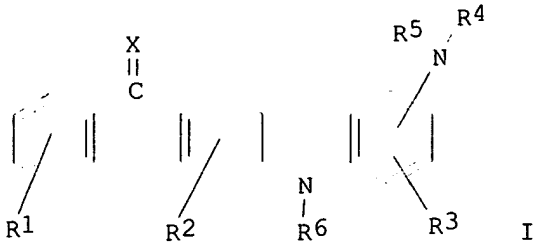



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:612095 HCAPLUS
DN 129:244921
TI Preparation of aromatic sulfonyl alpha-hydroxy hydroxamic acid compounds as matrix metalloprotease inhibitors
IN Freskos, John N.; Boehm, Terri L.; Mischke, Brent V.; Heintz, Robert M.; Mcdonald, Joseph J.; Decrescenzo, Gary A.; Howard, Susan C.
PA Monsanto Company, USA
SO PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | WO 9839326 | A1 | 19980911 | WO 1998-US4277 | 19980304 | |
| | W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | | |
| | AU 9864478 | A1 | 19980922 | AU 1998-64478 | 19980304 | <-- |
| | AU 737329 | B2 | 20010816 | | | |
| | EP 984959 | A1 | 20000315 | EP 1998-910177 | 19980304 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | | |
| | BR 9808150 | A | 20000328 | BR 1998-8150 | 19980304 | |
| | US 6362183 | B1 | 20020326 | US 1999-254535 | 19990604 | <-- |
| PRAI | US 1997-35182P | P | 19970304 | <-- | | |
| | WO 1998-US4277 | W | 19980304 | | | |

OS MARPAT 129:244921
AB The title compds. HONHC(O)C(OH)(R2)CH2SO2R1 [I; R2 = H, C1-4 alkyl, C1-4 haloalkyl, etc.; R1 = 5-6 membered cycloalkyl, heterocyclyl, aryl, etc.] which inter alia inhibit matrix metalloprotease activity, were prepd. Thus, multi-step synthesis of I [R1 = 4-PhOC6H4; R2 = Me] which showed 51.9% inhibition of angiogenesis in the cornea of a mouse, was described.
IT **213183-96-1P 213184-00-0P 213184-01-1P**
**213184-03-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. sulfonyl alpha-hydroxy hydroxamic acid compds. as matrix metalloprotease inhibitors)



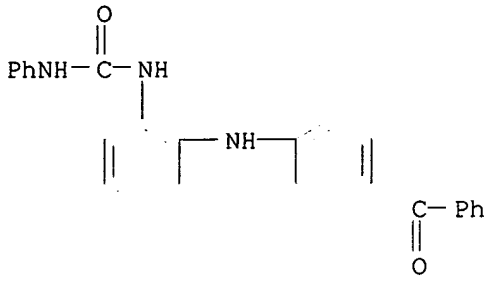
AB The title compds. I [R1 and R2 stand independently for one or more, similar or different substituents selected from the group consisting of hydrogen, halogen, hydroxy, mercapto, trifluoromethyl, amino, alkyl, alkoxy, alkylthio, alkylamino, or alkoxycarbonyl, the C-content of which can be from 1 to 5, cyano, carboxy, carbamoyl, Ph, or nitro; R3 stands for hydrogen, halogen, hydroxy, mercapto, trifluoromethyl, amino, alkyl, alkoxy, alkylthio, alkylamino, or alkoxycarbonyl, the C-content of which can be from 1 to 5, Ph, cyano, carboxy, or carbamoyl; R4, R5 and R6 stand independently for hydrogen, trifluoromethyl, alkyl, carbamoyl, alkoxycarbonyl, or alkyloxo, the C-content of which can be from 1 to 5; X stands for oxygen, NOH, NO-alkyl, dialkoxy, cyclic dialkoxy, dialkylthio, or cyclic dialkylthio, the C-content of which can be from 1 to 5] are prepd. The present compds. are of value in the human and veterinary practice as systemic and topical therapeutic agents for the treatment and prophylaxis of asthma, allergy, rheumatoid arthritis, spondyloarthritis, gout, atherosclerosis, chronic inflammatory bowel disease, **proliferative** and inflammatory skin disorders, such as psoriasis, and atopic dermatitis. In an in vitro test using human polymorphonuclear granulocytes, 4-(2-aminophenylamino)-2-chloro-2'-methylbenzophenone in vitro showed IC50 of 13 nM and 7.1 nM against the prodn. of Il-1.beta. and TNF-.alpha., resp. In the above test, 4-(2-aminophenylamino)benzophenone (II) in vitro showed IC50 of 250 nM and 790 nM against the prodn. of Il-1.beta. and TNF-.alpha., resp. In the 12-O-tetradecanoylphorbol-13-acetate induced murine skin inflammation model, II showed activity equal to hydrocortisone.

IT **210965-94-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminobenzophenones as inhibitors of interleukin and TNF)

IT **210965-94-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminobenzophenones as inhibitors of interleukin and TNF)

RN 210965-94-9 HCAPLUS

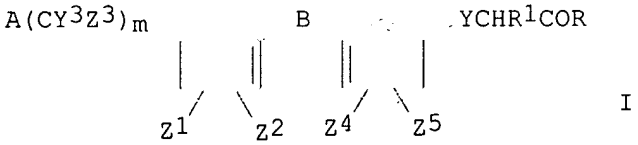
CN Urea, N-[2-[(4-benzoylphenyl)amino]phenyl]-N'-phenyl- (9CI) (CA INDEX NAME)



L74 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:430106 HCAPLUS
DN 129:108912
TI Preparation of 3-guanidinophenylamides and related compounds as integrin .alpha.v.beta.3 inhibitors or antagonists.
IN Chandrakumar, Nizal; Chen, Barbara B.; Chen, Helen Y.; Clare, Michael; Gasiecki, Alan F.; Haack, Richard A.; Malecha, James W.; Ruminski, Peter G.; Russell, Mark A.
PA G. D. Searle & Co., USA
SO U.S., 77 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5773646 | A | 19980630 | US 1997-825086 | 19970327 <-- |

OS MARPAT 129:108912
GI



AB Title compds. [I; A = NR5C(Y1)NR7R8, etc.; Y1 = NR2, O, S; R2 = H, alkyl, aryl, OH, alkoxy, cyano, NO2, amino, aminocarbonyl, alkenyl, alkynyl, (substituted) alkyl, aryl, heterocyclyl; R2R7 = (substituted) heterocyclyl; R7, R8 = H, alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, bicycloalkyl, aryl, acyl, benzoyl, (substituted) alkyl, heterocyclyl, etc.; NR7R8 = (substituted) mono- or bicyclic heterocyclyl; R5 = H, alkyl, alkenyl, alkynyl, PhCH2, PhCH2CH2; Z1, Z2, Z4, Z5 = H, alkyl, OH, alkoxy, aryloxy, aralkoxy, halo, haloalkyl, haloalkoxy, NO2, amino, aminoalkyl, alkylamino, dialkylamino, cyano, alkylthio, alkylsulfonyl, carboxyl derivs., (fused) aryl; cycloalkyl, (fused) heterocyclyl, A; B = SO2NR50, CONR50(CH2)p, CH2O, SOCH2, SO2CH2, etc.; p = 0-2; R50 = H, alkyl; Y = (CHR70)q, O; q = 0, 1; R70 = H, alkyl, (substituted) aryl; m = 0-2; R = XR3; X = O, S, NR4; R3, R4 = H, alkyl, alkenyl, alkynyl, halolalkyl, aryl, aralkyl, etc.; Y3, Z3 = H, alkyl, aryl, cycloalkyl, aralkyl; R1 = H, alkyl, aryl, etc.], were prepd. Thus, 3-[[[3-[(aminomiminomethyl)amino]phenyl]sulfonyl]amino]-.beta.-phenylbenzenepropanoic acid trifluoroacetate (prepn. given) inhibited vitronectin adhesion with IC50 = 16.7 nM.

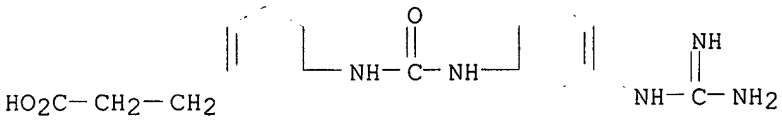
IT **197790-95-7P 197790-96-8P 197790-97-9P 197790-98-0P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-guanidinophenylamides and related compds. as integrin inhibitors or antagonists)

IT **197792-61-3P 197792-62-4P 197792-63-5P**
**197792-64-6P 197792-65-7P 197792-66-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 3-guanidinophenylamides and related compds. as integrin inhibitors or antagonists)

IT **197790-95-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-guanidinophenylamides and related compds. as integrin inhibitors or antagonists)

RN 197790-95-7 HCAPLUS
CN Benzenepropanoic acid, 3-[[[[3-[(aminoiminomethyl)amino]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



L74 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:331368 HCAPLUS
DN 129:4502
TI Preparation of guanylhydrazones and their use to treat inflammatory conditions
IN Bianchi, Marina; Cerami, Anthony; Tracey, Kevin J.; Ulrich, Peter
PA Picower Institute for Medical Research, USA
SO U.S., 44 pp. Cont.-in-part of U.S. 5,599,984.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|---|
| PI | US 5750573 | A | 19980512 | | US 1995-463568 | 19950605 | <-- |
| | US 5599984 | A | 19970204 | | US 1994-315170 | 19940929 | <-- |
| | US 5753684 | A | 19980519 | | US 1995-471696 | 19950606 | <-- |
| | US 5849794 | A | 19981215 | | US 1995-472004 | 19950606 | <-- |
| | US 5859062 | A | 19990112 | | US 1995-471124 | 19950606 | <-- |
| | US 6008255 | A | 19991228 | | US 1995-471305 | 19950606 | <-- |
| | US 6022900 | A | 20000208 | | US 1995-471919 | 19950606 | <-- |
| | US 6180676 | B1 | 20010130 | | US 1995-472003 | 19950606 | <-- |
| | US 6248787 | B1 | 20010619 | | US 1995-479050 | 19950606 | <-- |
| | US 5854289 | A | 19981229 | | US 1996-632305 | 19960415 | <-- |
| | US 2002028851 | A1 | 20020307 | | US 2001-824217 | 20010403 | <-- |
| PRAI | US 1994-184540 | B2 | 19940121 | <-- | | | |
| | US 1994-315170 | A2 | 19940929 | <-- | | | |
| | US 1995-463568 | A3 | 19950605 | <-- | | | |
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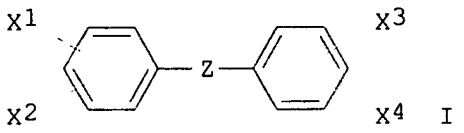
OS MARPAT 129:4502
GI



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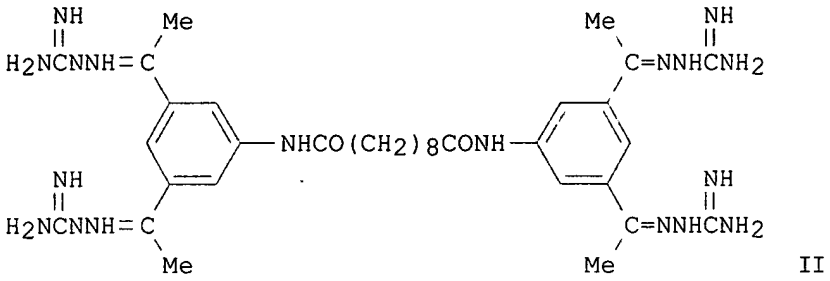


II

AB Arom. guanylhydrazone (more properly termed amidinohydrazone) [I; X2 = GhyCH, GhyCCH3 or H, wherein Ghy = guanylhydrazono; X1, X3 and X4, independently = GhyCH or GhyCCH3; and Z = NH(CO)NH] are prepd. This invention concerns new methods and compns. that are useful in preventing and ameliorating cachexia, the clin. syndrome of poor nutritional status and bodily wasting assocd. with **cancer** and other chronic diseases. More particularly, the invention relates to compns. contg. amidinohydrazone I and their use to inhibit the uptake of arginine by macrophages and/or its conversion to urea. These compns. and methods are also useful in preventing the generation of nitric oxide (NO) by cells, and so to prevent NO-mediated inflammation and other responses in persons in need of same. In another embodiment, the compds. I can be used to inhibit arginine uptake in arginine-dependent **tumors** and infections. Thus, N,N'-bis(3,5-diacetylphenyl)decanediamide, aminoguanidine hydrochloride, and aminoguanidine dihydrochloride were heated in 91% ethanol for 18 h to give the title compd. (II). II was the most active compd. in vitro for inhibiting urea prodn. in RAW 264.7 cell with IC50 of 1 .mu.M.

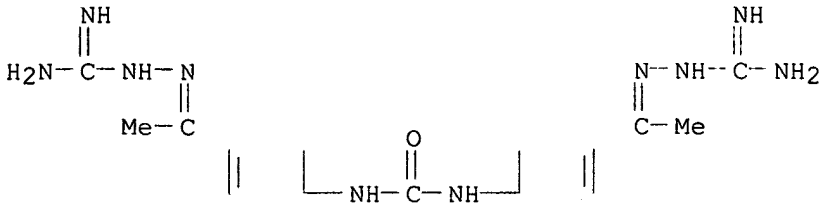
IT **15427-75-5P 169764-82-3P 169765-12-2P 169765-13-3P 187959-61-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of guanylhydrazones for treating NO- or arginine-mediated diseases such as inflammatory conditions)

IT **169765-14-4P 169765-32-6P 169765-36-0P 169765-37-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of guanylhydrazones for treating NO- or arginine-mediated diseases such as inflammatory conditions)

IT **15427-75-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of guanylhydrazones for treating NO- or arginine-mediated diseases such as inflammatory conditions)

RN 15427-75-5 HCAPLUS

CN Hydrazinecarboximidamide, 2,2'-[carbonylbis(imino-4,1-phenyleneethylidyne)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L74 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:805714 HCAPLUS
DN 128:61354
TI Preparation of arylureas and related compounds as chloride channel blockers.
IN Christophersen, Palle; Pedersen, Ove
PA Neurosearch A/S, Den.; Christophersen, Palle; Pedersen, Ove
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9745400 | A1 | 19971204 | WO 1997-EP2723 | 19970526 <-- |
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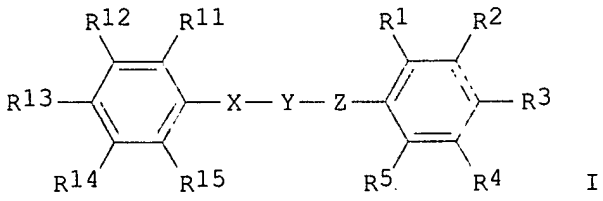
| | RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9729621 | A1 | 19980105 | AU 1997-29621 | 19970526 <-- |
| | AU 735545 | B2 | 20010712 | | |
| | EP 906273 | A1 | 19990407 | EP 1997-924019 | 19970526 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 2000511167 | T2 | 20000829 | JP 1997-541595 | 19970526 <-- |
| PRAI | DK 1996-602 | A | 19960524 <-- | | |
| | DK 1997-452 | A | 19970422 <-- | | |
| | WO 1997-EP2723 | W | 19970526 <-- | | |

OS MARPAT 128:61354
GI



I

AB Title compds. [I; 1 of R1, R2, R3 = non-cyclic acidic group having a pKa

value <8 or a group in vivo convertible thereto; R4, R5, and the other 2 of R1, R2, R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxy, hydroxy, halo, CF3, OCF3, cyano, NO2, amino, (substituted) aryl, aralkyl, arylamino, aryloxy, arylcarbonyl, heteroaryl; R3R4 or R4R5 = (unsatd.) fused 4-7 membered carbocyclic ring; X = NH, CH2NH, SO2NH; Y = CO, CS, SO2, C(:NR8); R8 = H, alkyl, cyano; X = NH, CH2NH, SO2NH; Z = NR6, O, CH:CH, C.tplbond.C, N:CH, CH:N; R6 = H, alkyl; R11-R15 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxy, OH halo, CF3, OCF3, cyano, NO2, amino, NHSO2R7, CO2R7, SO2N(R7)2, SO2OR7, etc.], were prepd. Thus, 3-trifluoromethylphenyl isocyanate and 2-aminobenzoic acid were kept in toluene to give N-(3-trifluoromethylphenyl)-N'-(2-carboxyphenyl)urea. The latter at 10 .mu.M normalized the basal K+ flux from sickle erythrocytes and nearly abolished the deoxygenation induced flux component.

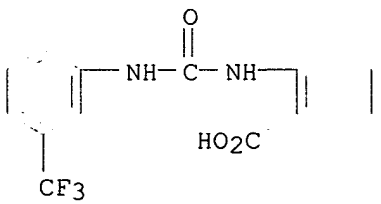
IT **1566-81-0P 1566-82-1P 1566-85-4P**
**1566-86-5P 1566-88-7P 1566-98-9P**
**54506-39-7P 160384-12-3P 160384-14-5P**
**160384-23-6P 182958-17-4P 195133-45-0P**
**200193-39-1P 200193-40-4P 200193-41-5P**
**200193-42-6P 200193-43-7P 200193-44-8P**
**200193-45-9P 200193-46-0P 200193-47-1P**
**200193-48-2P 200193-49-3P 200193-50-6P**
**200193-52-8P 200193-53-9P 200193-56-2P**
**200193-57-3P 200193-58-4P 200193-59-5P**
**200193-60-8P 200193-62-0P 200193-63-1P**
**200193-64-2P 200193-65-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylureas and related compds. as chloride channel blockers)

IT **200193-72-2**
RL: RCT (Reactant)
(prepn. of arylureas and related compds. as chloride channel blockers)

IT **200193-73-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of arylureas and related compds. as chloride channel blockers)

IT **1566-81-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylureas and related compds. as chloride channel blockers)

RN 1566-81-0 HCAPLUS
CN Benzoic acid, 2-[[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)




L74 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:679052 HCAPLUS
DN 127:318772
TI Preparation of meta-substituted phenylene derivatives and their use as .alpha.v.beta.3 integrin antagonists or inhibitors
IN Chandrakumar, Nizal; Chen, Barbara B.; Chen, Helen; Clare, Michael; Gasiecki, Alan F.; Haack, Richard A.; Malecha, James W.; et al.

PA G.D. Searle & Co., USA; Chandrakumar, Nizal; Chen, Barbara B.; Chen, Helen; Clare, Michael; Gasiecki, Alan F.

SO PCT Int. Appl., 306 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9736862 | A1 | 19971009 | WO 1997-US4461 | 19970326 <-- |
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| | RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2250464 | AA | 19971009 | CA 1997-2250464 | 19970326 <-- |
| | AU 9723370 | A1 | 19971022 | AU 1997-23370 | 19970326 <-- |
| | EP 889877 | A1 | 19990113 | EP 1997-916110 | 19970326 <-- |
| | EP 889877 | B1 | 20010829 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| | JP 2000506538 | T2 | 20000530 | JP 1997-535309 | 19970326 <-- |
| | AT 204857 | E | 20010915 | AT 1997-916110 | 19970326 <-- |
| | ES 2162676 | T3 | 20020101 | ES 1997-916110 | 19970326 <-- |
| PRAI | US 1996-14464P | P | 19960329 <-- | | |
| | WO 1997-US4461 | W | 19970326 <-- | | |

OS MARPAT 127:318772

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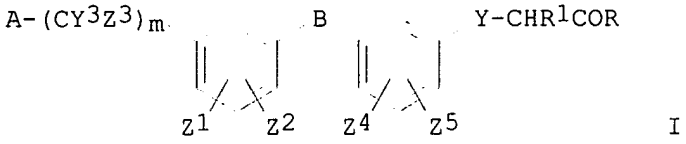


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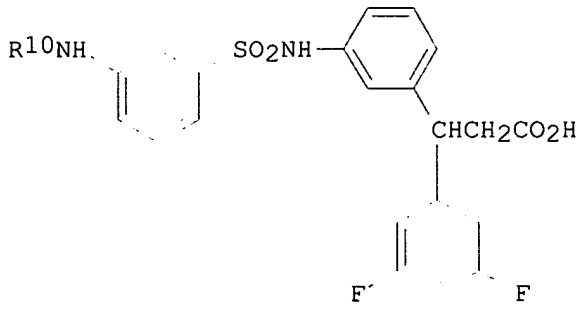
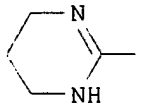



II

Q= 


AB The present invention relates to a class of compds., i.e, phenylalkanoic acid and phenoxyacetic acid derivs., represented by formula [I; A =

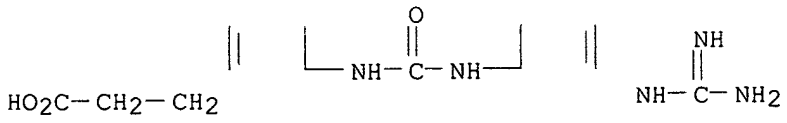
(un)substituted NHC(:NH)NH, NHCONH, NHC(:S)NH, or NHCH:NH, C(:NH)NH2, C(:NOH)NH2; Z1 - Z5 = H, alkyl, OH, alkoxy, aryloxy, aralkoxy, halo, haloalkyl, haloalkoxy, NO2, NH2, aminoalkyl, alkylamino, dialkylamino, cyano, etc.; B = N-(un)substituted CONH(CH2)p or SO2NH, NHCONH(CH2)p, CO2(CH2)p, CH2CH2, alkenylene or alkynylene optionally substituted by oxo, CH2O, SCH2, SOCH2, SO2 CH2, CH(OH)CH2O, CH:CHCO; wherein p = 0, 1,2; Y = (un)substituted (CH2)q, O; q = 0,1; m = 0, 1,2; R = X-R3; wherein X = O, S, (un)substituted NH; R3 = H, alkyl, alkenyl, alkynyl, haloalkyl, aryl, aralkyl, sugar or steroid residue; Y3, Z3 = H, alkyl, aryl, cycloalkyl, aralkyl; R1 = H, alkyl, aryl, NHCOR51, NHCO2R12, NHCOR12, NHSO2R12, NHCONHR12; wherein R12 = H, alkyl, cycloalkyl, aralkyl, aryl; R51 = N-substituted pyrrolidinyl, piperidinyl, or morpholinyl] or pharmaceutically acceptable salts thereof are prepd. Also claimed are pharmaceutical compns. comprising above compds. I and methods of selectively inhibiting or antagonizing .alpha.v.beta.3 integrin. A method for treating conditions mediated by .alpha.v.beta.3 integrin, e.g. **tumor metastasis**, solid **tumor** growth, angiogenesis, osteoporosis, humoral hypercalcemia of **malignancy**, smooth muscle cell migration, restenosis, in a mammal comprises administering an effective .alpha.v.beta.3 integrin-inhibiting amt. of above compds. I. Thus, 3-(3-aminobenzenesulfonamido)-3-phenylpropanoic acid deriv. (II; R10 = H) was condensed with N,N'-bis(tert-butoxycarbonyl)-2-(1H)-tetrahydropyrimidinethione followed by deprotection to give II (R10 = Q), which showed IC50 of 0.75 nM for 50% inhibition of the max. binding of biotinylated vitronectin to human vitronectin receptor (.alpha.v.beta.3) purified from human placenta (Niiya et al., Blood, 1987).

IT **197790-95-7P 197790-96-8P 197790-97-9P**
**197790-98-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of meta-substituted phenylene derivs. and their use as .alpha.v.beta.3 integrin antagonists or inhibitors for disease treatment)

IT **197792-61-3P 197792-62-4P 197792-63-5P**
**197792-64-6P 197792-65-7P 197792-66-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of meta-substituted phenylene derivs. and their use as .alpha.v.beta.3 integrin antagonists or inhibitors for disease treatment)

IT **197790-95-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of meta-substituted phenylene derivs. and their use as .alpha.v.beta.3 integrin antagonists or inhibitors for disease treatment)

RN 197790-95-7 HCAPLUS
CN Benzenepropanoic acid, 3-[[[[3-[(aminoiminomethyl)amino]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



L74 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:679049 HCAPLUS
DN 127:346198

TI Para-substituted phenylpropanoic acid derivatives prepared as integrin antagonists

IN Chen, Barbara B.; Chen, Helen Y.; Gesicki, Glen J.; Haack, Richard A.; Malecha, James W.; Penning, Thomas D.; Rico, Joseph G.; Rogers, Thomas E.; et al.

PA G.D. Searle & Co., USA; Chen, Barbara B.; Chen, Helen Y.; Gesicki, Glen J.; Haack, Richard A.; Malecha, James W.; Penning, Thomas D.

SO PCT Int. Appl., 359 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9736859 | A1 | 19971009 | WO 1997-US4460 | 19970326 <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2250698 | AA | 19971009 | CA 1997-2250698 | 19970326 <-- |
| | AU 9725360 | A1 | 19971022 | AU 1997-25360 | 19970326 <-- |
| | EP 891325 | A1 | 19990120 | EP 1997-916852 | 19970326 <-- |
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| | JP 2000515493 | T2 | 20001121 | JP 1997-535308 | 19970326 <-- |
| | EP 1157985 | A1 | 20011128 | EP 2001-114256 | 19970326 <-- |
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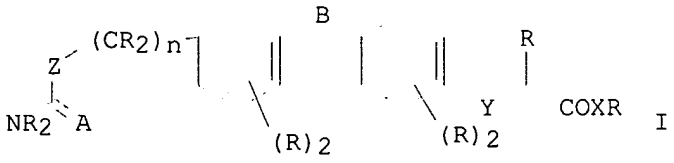
| | US 6251944 | B1 | 20010626 | US 1999-288742 | 19990408 <-- |
| PRAI | US 1996-14288P | P | 19960329 <-- | | |
| | EP 1997-916852 | A3 | 19970326 <-- | | |
| | WO 1997-US4460 | W | 19970326 <-- | | |
| | US 1997-826244 | A3 | 19970327 <-- | | |

OS MARPAT 127:346198

GI




AB The present prepn. relates to a class of racemic, L-, or D-compds. [I; A = O, S, NH, NOH, NR; R = H, OH, alkyl, aryl, nitro, amino; B = CH2CONH, COO, SO2NH, CH2O, OCH2; Z = bond, NR; Y = O, S, SO2; X = O, S, N; n = 0-2; etc.] or a pharmaceutically acceptable salt thereof, which offers treatment of disease states, including angiogenesis (no data).

IT **198150-78-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(4-substituted phenylpropanoic acid derivs. prepd. as integrin antagonists)

IT **198150-77-5P 198152-76-0P 198152-77-1P 198152-78-2P 198152-79-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(4-substituted phenylpropanoic acid derivs. prepd. as integrin antagonists)

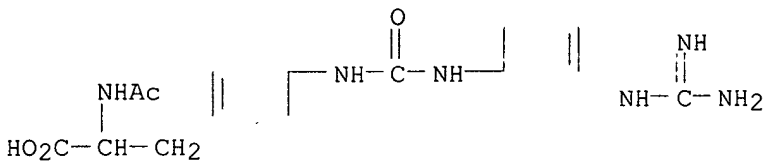
IT **198150-78-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(4-substituted phenylpropanoic acid derivs. prepd. as integrin antagonists)

RN 198150-78-6 HCAPLUS

CN Phenylalanine, N-acetyl-4-[[[[3-[(aminoiminomethyl)amino]phenyl]amino]carbonyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

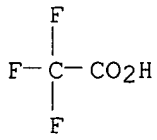
CM 1

CRN 198150-77-5
CMF C19 H22 N6 O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L74 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:124926 HCAPLUS

DN 126:211914

TI Preparation of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases.

IN Bianchi, Marina; Cerami, Anthony; Tracey, Kevin J.; Ulrich, Peter

PA Picower Institute for Medical Research, USA

SO U.S., 42 pp. Cont.-in-part of U.S. Ser. No. 184,540, abandoned.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 5599984 | A | 19970204 | US 1994-315170 | 19940929 <-- |
| CA 2181689 | AA | 19950727 | CA 1995-2181689 | 19950119 <-- |
| WO 9519767 | A1 | 19950727 | WO 1995-US828 | 19950119 <-- |

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RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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| | AU 9518330 | A1 | 19950808 | AU 1995-18330 | 19950119 <-- |
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| | EP 1160240 | A1 | 20011205 | EP 2001-112374 | 19950119 <-- |
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| | US 5849794 | A | 19981215 | US 1995-472004 | 19950606 <-- |
| | US 5859062 | A | 19990112 | US 1995-471124 | 19950606 <-- |
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OS MARPAT 126:211914

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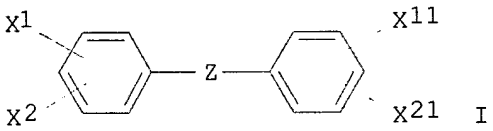



I

AB Title compds., e.g. [I; X2 = H, Q1, Q2; X1, X11, X21 = Q1, Q2; Z = NHCONH, C6H4, C5NH3, A(CH2)nA; n = 2-10; A = NHCO, NHCONH, NH, O; Q1 = H2N(CNH)NHN:CH, H2N(CNH)NHN:CMe], were prepd. Thus, N,N'-bis(3,5-diacetylphenyl)decanediamide (prepn. given), aminoguanidine hydrochloride, and aminoguanidine dihydrochloride were heated in EtOH for 18 h to give N,N'-bis(3,5-diacetylphenyl)decanediamide tetrakis(amidinohydrazone) tetrahydrochloride. The latter at 200 .mu.M gave 100% inhibition of urea prodn., NO2/NO3 prodn., and arginine transport in activated macrophages.

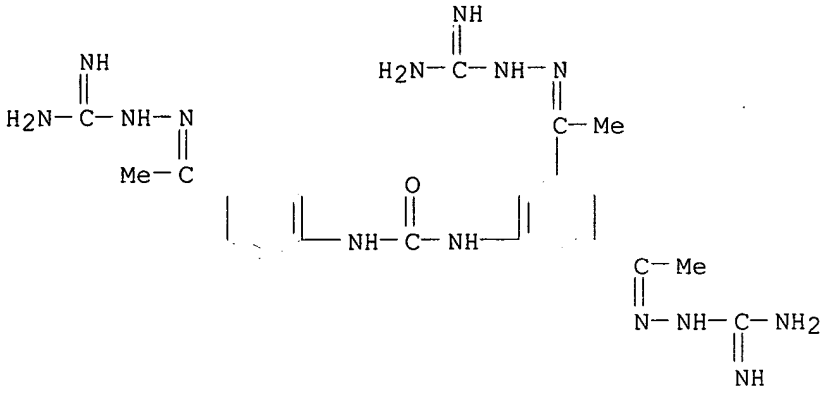
IT **169764-82-3P 169765-12-2P 169765-13-3P**
**187959-61-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases)

IT **169765-14-4P 169765-32-6P 169765-36-0P**
**169765-37-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases)

IT **169764-82-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases)

RN 169764-82-3 HCAPLUS

CN Hydrazinecarboximidamide, 2,2'-[[5-[[[[4-[1-[(aminoiminomethyl)hydrazono]ethyl]phenyl]amino]carbonyl]amino]-1,3-phenylene]diethylidyne]bis-, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

L74 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:662389 HCAPLUS
DN 123:55495
TI Preparation of ureiodobenzoylguanidines as sodium-proton antiporter inhibitors
IN Schwark, Jan-Robert; Lang, Hans-Jochen; Kleemann, Heinz-Werner; Weichert, Andreas; Scholz, Wolfgang; Albus, Udo
PA Hoechst A.-G., Germany
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | EP 638548 | A1 | 19950215 | EP 1994-112383 | 19940808 | <-- |
| | EP 638548 | B1 | 19980422 | | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | | |
| | DE 4327244 | A1 | 19950216 | DE 1993-4327244 | 19930813 | <-- |
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| | AU 683273 | B2 | 19971106 | | | |
| | CN 1111618 | A | 19951115 | CN 1994-109503 | 19940811 | <-- |
| | CN 1060763 | B | 20010117 | | | |
| | US 5559153 | A | 19960924 | US 1994-289674 | 19940811 | <-- |
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| | HU 71816 | A2 | 19960228 | HU 1994-2346 | 19940812 | <-- |
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OS MARPAT 123:55495

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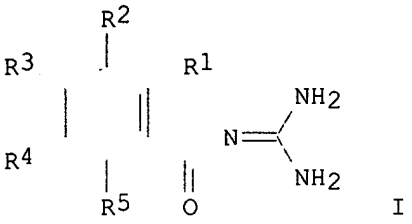


AB Title compds. [I; 1 of R1,R3,R4 = NR6C(:X)NR7R8 and the others = H, halo, alk(en)yl(oxy), etc.; R6-R8 = H, (perfluoro)alkyl, alkenyl, etc.] were prepd. Thus, 5-chloroisatoic anhydride was condensed with N-trimethylsilylpiperidine and the product condensed with (H2N)2C:NH to give I (R1 = piperidinocarbonylamino, R2 = R3 = R5 = H, R4 = Cl) which had IC50 of 1-2.mu.M against rabbit erythrocyte Na+/H+-exchangers in vitro.

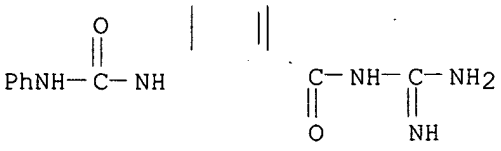
IT **164653-11-6P 164653-17-2P 164653-23-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ureiodobenzoylguanidines as sodium-proton antiporter inhibitors)

IT **164653-32-1P 164653-36-5P 164653-41-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of ureiodobenzoylguanidines as sodium-proton antiporter inhibitors)

IT **164653-11-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ureiodobenzoylguanidines as sodium-proton antiporter inhibitors)

RN 164653-11-6 HCAPLUS

CN Benzamide, N-(aminoiminomethyl)-3-[[(phenylamino)carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L74 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1987:477448 HCAPLUS

DN 107:77448

TI Preparation of isophthalonitrile derivatives as agricultural bactericides

IN Ishikawa, Nobuo; Motoyoshi, Masatoshi

PA SDS Biotech Corp., Japan

SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF

DT Patent

LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 62081361 | A2 | 19870414 | JP 1985-220167 | 19851004 <-- |

OS CASREACT 107:77448
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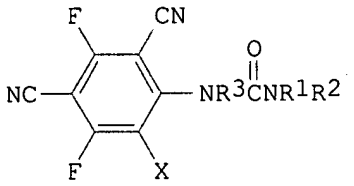


I

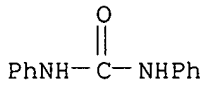
AB The title compds. I [X = Cl, F; R1, R2, R3 = H, alkyl, (un)substituted Ph], useful as agricultural antimicrobial agents, are prepd. A soln. of 2.00 g tetrafluoroisophthalonitrile and 1.11 g H2NCONHMe in 1,4-dioxane was refluxed for 12 h to give 80.7% I (R1 = Me; R2 = R3 = H; X = F), whose MIC (ppm) against Penicillium funiculosum, Aspergillus niger, Fusarium **proliferatum**, Gliocladium virens, and Rhizopus stolonifer are 50, 50, 50, 100, and 50, resp., vs. 5, 5, 500, >500, and 500 ppm for chlorothalonil.

IT **102-07-8**
RL: RCT (Reactant)
(arylation of, with tetrafluoroisophthalonitrile)

IT **109678-91-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as agricultural bactericide and fungicide)

IT **102-07-8**
RL: RCT (Reactant)
(arylation of, with tetrafluoroisophthalonitrile)

RN 102-07-8 HCAPLUS
CN Urea, N,N'-diphenyl- (9CI) (CA INDEX NAME)



L74 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1986:626077 HCAPLUS
DN 105:226077
TI Benzoylurea compounds and **antitumor** compositions containing them
IN Haga, Takahiro; Yamada, Nobutoshi; Sugi, Hideo; Koyanagi, Toru; Kondo, Nobuo; Nakajima, Tsunetaka; Watanabe, Masahiro; Yokoyama, Kazumasa
PA Ishihara Sangyo Kaisha, Ltd., Japan
SO Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| PI | EP 192235 | A1 | 19860827 | EP 1986-102063 | 19860218 <-- |
| | EP 192235 | B1 | 19891123 | | |

R: BE, CH, DE, FR, GB, IT, LI, NL, SE

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| | JP 01056065 | B4 | 19891128 | | |
| | US 4727077 | A | 19880223 | US 1986-823521 | 19860129 <-- |
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| | ZA 8600775 | A | 19861029 | ZA 1986-775 | 19860203 <-- |
| | GB 2171695 | A1 | 19860903 | GB 1986-2792 | 19860205 <-- |
| | GB 2171695 | B2 | 19890105 | | |
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| | DK 163124 | B | 19920120 | | |
| | DK 163124 | C | 19920609 | | |
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OS CASREACT 105:226077

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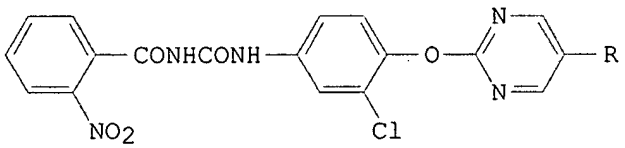


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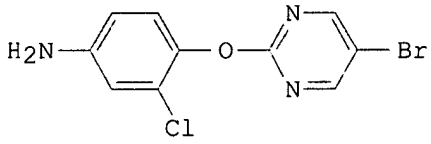


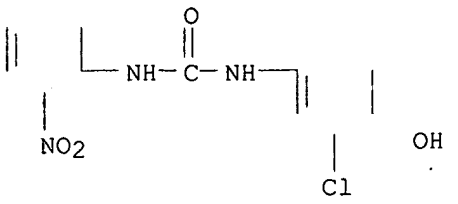

II

AB Title compds. I (R = Br, Cl) were prepd. as **antitumor** agents. Thus, 5-bromo-2-chloropyrimidine and 2,4-Cl(H2N)C6H3OH were condensed in Me2SO contg. K2CO3 to give pyrimidinyloxyaniline II, which was treated with 2-O2NC6H4CONCO to give I (R = Br) (III). I (R = Cl) (IV) was similarly prepd., and III was also prepd. by 2 other methods. Against leukemia P-388 in mice, III and IV showed i.p. activity inferior or comparable to the known compd. I (R = iodo), but showed markedly superior oral activity. A liposomal formulation was prepd. from III 5, yolk phospholipid 2, .alpha.-tocopherol 0.001, and physiol. saline 92.999 wt. parts.

IT **105355-39-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with bromochloropyrimidine)

IT **105355-39-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with bromochloropyrimidine)

RN 105355-39-3 HCAPLUS
CN Urea, N-(3-chloro-4-hydroxyphenyl)-N'-(2-nitrophenyl)- (9CI) (CA INDEX NAME)



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L3 2 S L2 AND C22H23N3O2/MF
L4 23424 S L2 NOT L3

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L5 8315 S L4

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L7 297 S L6
L8 546 S RAF KINASE OR C RAF KINASE OR PROTEIN KINASE C RAF OR GENE C
L9 17 S KINASE PHOSPHORYLATING GENE C RAF PROTEIN
L10 574 S L7-L9
L11 7 S L5 AND L10

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L12 11 S (L8 OR L9) NOT L6

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L13 143 S L12
L14 1 S L5 AND L13
L15 7 S L11,L14
L16 6950 S L5 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L17 5 S L15 AND L16
E BAYER/PA,CS
L18 197 S E3,E4 AND L5
E MILLER S/AU
L19 930 S E3-E36
E MILLER SCOTT/AU
L20 222 S E3-E26
E OSTERHOUT M/AU
L21 34 S E3-E5,E7-E9
E DUMAS J/AU
L22 458 S E3-E16
E KHIRE U/AU

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L24          23 S E4-E6
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L25          84 S E3,E7
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L26         155 S E3,E22-E27
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L27         153 S E3,E34-E39
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L28         992 S E3-E15
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                E GUNN D/AU
L32          33 S E3,E6,E15,E16
                E RODRIGUEZ M/AU
L33         942 S E3-E70,E242-E251
                E WANG M/AU
L34        1245 S E3-E34
                E WANG MING/AU
L35        2083 S WANG MING?/AU
                E TURNER T/AU
L36         358 S E3-E23
                E TURNER TIFFANY/AU
L37           1 S E3
                E BRENNAN C/AU
L38          74 S E3-E13,E21-E25
L39          18 S L5 AND L19-L38
L40          10 S L16 AND L39
                E GUNN DAVID/AU
L41          10 S E3
L42           3 S L41 AND L5
L43           2 S RODRIGUEZ M?/AU AND L5
L44           7 S L39,L42,L43,L18 AND L15
L45           5 S L16 AND L44
L46           2 S L44 NOT L45

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L53        1728 S L52 AND (1 OR 63)/SC,SX
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                E E5+ALL
L54         303 S L52 AND E4,E3+NT
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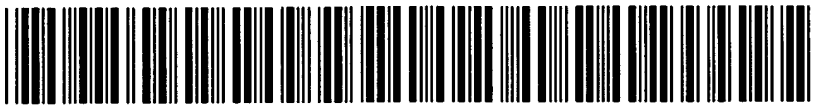
FILE 'HCAPLUS' ENTERED AT 11:38:35 ON 02 MAY 2002

L55 643 S L52 AND (?NEOPLAS? OR ?CANCER? OR ?CARCIN? OR ?TUMOR? OR ?TUM
L56 645 S L54,L55
L57 519 S L53 AND L56
L58 134 S L57 AND P/DT
L59 91 S L58 AND US/PC
L60 44 S L57 AND ?KINASE?
L61 19 S L60 AND L58
L62 1033 S L50 (L) THU/RL
L63 218 S L62 AND L57
L64 97 S L63 AND L58
L65 69 S L64 AND L59
L66 8 S L65 AND L60
L67 19 S L61,L66

FILE 'HCAPLUS' ENTERED AT 11:43:30 ON 02 MAY 2002

L68 262 S BENZEN?/SC AND L52
L69 79 S L68 AND L53
L70 11 S L68 AND L54
L71 16 S L68 AND L56
L72 13 S L68 AND L63
L73 15 S L69 AND L70-L72
L74 15 S L70-L73 NOT L67

US 097769360JP1



Creation date: 04-22-2004
Indexing Officer: JACKERMANWILSON - JEAN ACKERMAN-WILSON
Team: OIPEBackFileIndexing
Dossier: 09776936

Legal Date: 05-07-2002

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